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A RETROSPECTIVE ANALYSIS OF CSF AND CLINICAL PROFILES DIAGNOSED IN THE CASES OF PYOGENIC MENINGITIS (PM) AND TUBERCULOUS MENINGITIS (TBM) AT NISHTAR HOSPITAL, MULTAN

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Abstract:
Objectives: *Our research primarily aimed at the laboratory and clinical manifestation of the TB cum bacterial meningitis, the next aim of the research was ratio determination of the protein glucose in cerebrospinal fluid which can be helpful in the condition prediction.*
Methods: *Research design was retrospective which was carried out at Nishtar Hospital, Multan in the time span of Feb, 2016 to Dec, 2017 on the medical records of forty-six cases of the TB and thirty-three cases of the bacterial meningitis. TB meningitis is a disease which is referred to an of above the period of two weeks, tuberculoma and basal enhancement were identified through scan of computerized tomography and with the help of anti-TB therapy response. The definition of the pyogenic meningitis was made as pathogenic isolate response in the fluid of cerebrospinal (bacterial culture) or through a pathogen on cerebrospinal fluid gram stain or positive latex particle agglutination and antibiotic clinical improvements. We also used Logistic regression test for the TB meningitis probability. For the definition of the optimal protein-glucose proportion, diagnosis cutoff point of TB meningitis, with an application of curve of the receiver operating features. Data analysis was carried on SPSS.*
Results: *TB meningitis predictive features were diagnosed as protein to glucose ratio more than 2 (21, OR; CI, 95%; 4.7 – 93); total leukocyte count of the cerebrospinal fluid was under 800 (58, OR; CI, 95%; 5 – 649); and hydrocephalus presence as (19, OR; CI, 95%; 3.3 – 109).*
Conclusion: *We observed a set of simple laboratories, clinical and radiological criteria which can be helpful in the prediction of the TB meningitis. The cerebrospinal fluid value protein to glucose proportion requires validation in the large-scale research studies which can be confirmed through bacteriological TB meningitis case.*
Keywords: *Tuberculous (TB) meningitis, Protein to glucose ratio, Independent predictors and Pakistan.*

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INTRODUCTION:

Death is caused in majority of the cases of Tuberculosis (TB) which is a repeated children infection. It is estimated that 1/3rd population of the planet earth is infected with the TB Mycobacterium, developing countries face its burden as 75% [1]. An annual report of the TB cases is estimated as 9 – 10 million across the world, in which fifty percent of the cases are extrapulmonary [1]. Children face a higher incidence of TB than the adult population with complication rate of 0.3% as primary children infection [2].

TB has large scale mortality and morbidity rates in both the cases if treated or untreated as it is difficult to diagnose because no specific symptoms are associated with this infection and its signs also overlap many of the chronic and acute CNS (Central Nervous System) diseases [3]. Cerebrospinal fluid assessment is a vital clinical parameter in the meningitis diagnosis, but the abnormalities produced in CSF through bacterial pathogens, specifically in the partially managed patients are difficult for the TBM differentiation in the patients.

This situation is true in the early stage of the TBM as the evaluation of the protein is not associated and there may be a dominance of the neutrophils cells [4]. It is also reported in a research that early dominance of the neutrophil in CSF is elevated such as (36%) in the TBM patients [5]. A preliminary children TBM diagnosis which is made on the grounds of the clinical assessment and history, radiological outcomes and CSF. In the absence of mycobacteria isolation from clinical specimen (either CSF or sputum), diagnostic uncertainty is prevalent in this case which leads to an appropriate therapy initiation delay [6]. Large volumes of fluid are required in order to isolate CSF from the TB bacilli, with forty percent CSF sensitivity [7]. Effective and sophisticated tests which include Polymerase Chain Reaction (PCR) and Mycobacterium tuberculosis (MTB) have a decreased rate of the sensitivity for 40 – 60 percent pediatric group of age, they are expansive and less accessible in the under developed countries which increases the disease burden [8, 9].

Our research made an attempt for the evaluation of the set of laboratory and clinical parameters which are effective in the TBM prediction in the immunocompetent cases, where bacteriological confirmation is not present. Early diagnosis can be supportive for the management of TBM, that is a potential cause of adverse and severe outcomes.

MATERIALS AND METHODS:

Research design was retrospective which was carried out at Nishtar Hospital, Multan in the time span of Feb, 2016 to Dec, 2017 on the medical records of forty-six cases of the TB and thirty-three cases of the bacterial meningitis. TB meningitis is a disease which is referred to an of above the period of two weeks, tuberculoma and basal enhancement were identified through scan of computerized tomography and with the help of anti-TB therapy response. The definition of the pyogenic meningitis was made as pathogenic isolate response in the fluid of cerebrospinal (bacterial culture) or through a pathogen on cerebrospinal fluid gram stain or positive latex particle agglutination and antibiotic clinical improvements. We also categorized all the patients as bacterial and tuberculous meningitis on the basis of available hospital record and consulted literature [5].

Bacterial meningitis cases were managed with a course of ceftriaxone for ten to fourteen days; whereas, the TBM diagnosed cases were managed with four-drug regimen including steroids as prescribed by the guidelines of the WHO [1].

We also used Logistic regression test for the TB meningitis probability. For the definition of the optimal protein-glucose proportion, diagnosis cutoff point of TB meningitis, with an application of curve of the receiver operating features. Data analysis was carried on SPSS. Ethical approval and informed consent was taken before the commencement of the research.

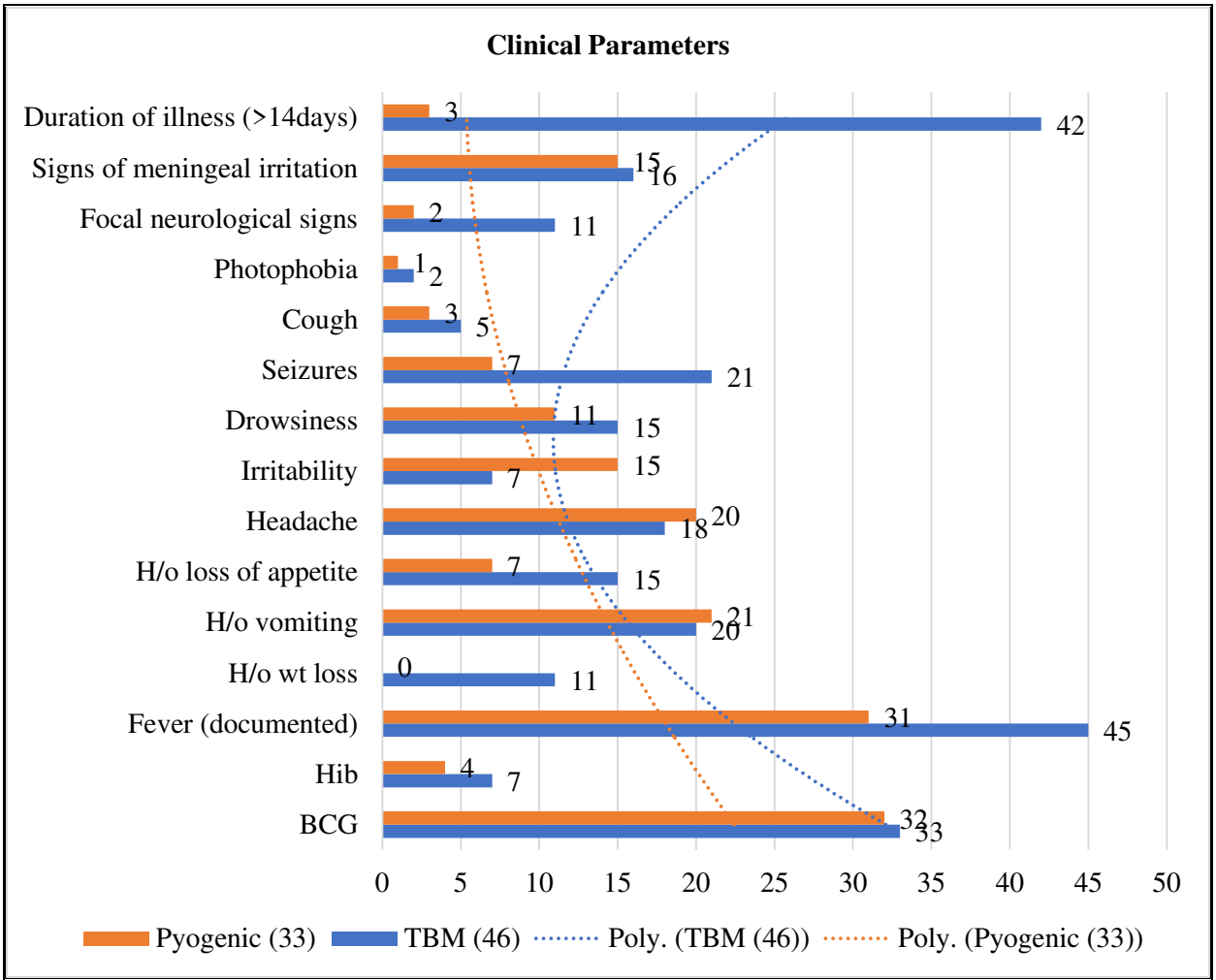
RESULTS:

TB meningitis predictive features were diagnosed as protein to glucose ratio more than 2 (21, OR; CI, 95%; 4.7 – 93); total leukocyte count of the cerebrospinal fluid was under 800 (58, OR; CI, 95%; 5 – 649); and hydrocephalus presence as (19, OR; CI, 95%; 3.3 – 109).

In the cases of pyogenic meningitis there was a common presentation of the irritability and headache. TBM cases were prolonged history above two weeks and also presented seizures, higher protein, lower glucose and focal neurological signs (in the CSF assessment) when compared to the pyogenic meningitis children (Table – I).

Table – I: Laboratory and Clinical Parameters Univariate Analysis of Pyogenic and TB Meningitis

Clinical parameters	**TBM (46)**	**Pyogenic (33)**	**Crude (OR)**
Male	27	23	
Mean age in months	67 ± 56	63.5 54	1.0 (0.9 – 1.0)
Mean weight (Kg)	17 ± 10	18.5 13	1.0 (0.9 – 1.0)
BCG	33	32	0.8(0.01 – 0.6)
Hib	7	4	1.3(0.35 – 5.0)
Fever (documented)	45	31	0.3 (0.03 – 4)
H/o weight loss	11	0	
H/o vomiting	20	21	0.4 (0.2 – 1.1)
H/o loss of appetite	15	7	1.8 (0.6 – 5)
Headache	18	20	0.4(0.2 – 1.0)
Irritability	7	15	0.2 (0.08 – 0.6)
Drowsiness	15	11	0.97 (0.3 – 2.5)
Seizures	21	7	3 (1.1 – 9)
Cough	5	3	1.2(0.3 – 5.5)
Photophobia	2	1	1.5 (0.1 – 16)
Focal neurological signs	11	2	5 (1 – 24)
Signs of meningeal irritation	16	15	0.6 (0.3 – 1.6)
Duration of illness (above 14 days)	42	3	105 (22 – 103)
Mean ESR (mm 1st hour)	19.5 (± 16.5)	31 (± 21)	0.9 (0.9 – 1.0)
Mean CRP	4 (± 8.5)	5.5 (± 8)	0.9 (0.9 – 1)
Mean TLC (10^9)	29 (± 96)	18 (± 8)	1.0 (0.9 – 1.0)
MT (mm)	06 to 12	0/1	
CSF Analysis			
Mean TLC (10^9)	268 (±757)	1064 (± 2513)	0.9 (0.9 – 1.0)
Mean Protein (mg/dl)	340 (± 606)	99 (± 80)	1.0(1.0 – 1.04)
Mean Glucose (mg/dl)	45 (± 21)	58 (± 23)	0.97 (0.9 – 1.0)
Protein: Glucose			
<2	7	23	13.0 (4.3 – 38)
≥2	39	10	
CT scan findings	**TBM (44)**	**Pyogenic (24)**	**Crude (OR)**
Basal meningeal enhancement	18	3	5.0 (1.3 – 18)
Hydrocephalus	29	4	9.6 (3 – 33)
Cerebral edema	9	3	2.0 (0.5 – 8)
Tuberculoma	9	0	6.2 (0.7 – 52)
Infarction	8	2	2.5 (0.5 – 13)


Clinical Parameters
Duration of illness (>14days)
Signs of meningeal irritation
Focal neurological signs
Photophobia
Cough
Seizures
Drowsiness
Irritability
Headache
H/o loss of appetite
H/o vomiting
H/o wt loss
Fever (documented)
Hib
BCG
3
42
15
16
2
11
1
2
3
5
7
21
11
15
15
7
20
18
7
15
21
20
0
11
31
45
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0 5 10 15 20 25 30 35 40 45 50
Pyogenic (33)
TBM (46)
Poly. (TBM (46))
Poly. (Pyogenic (33))

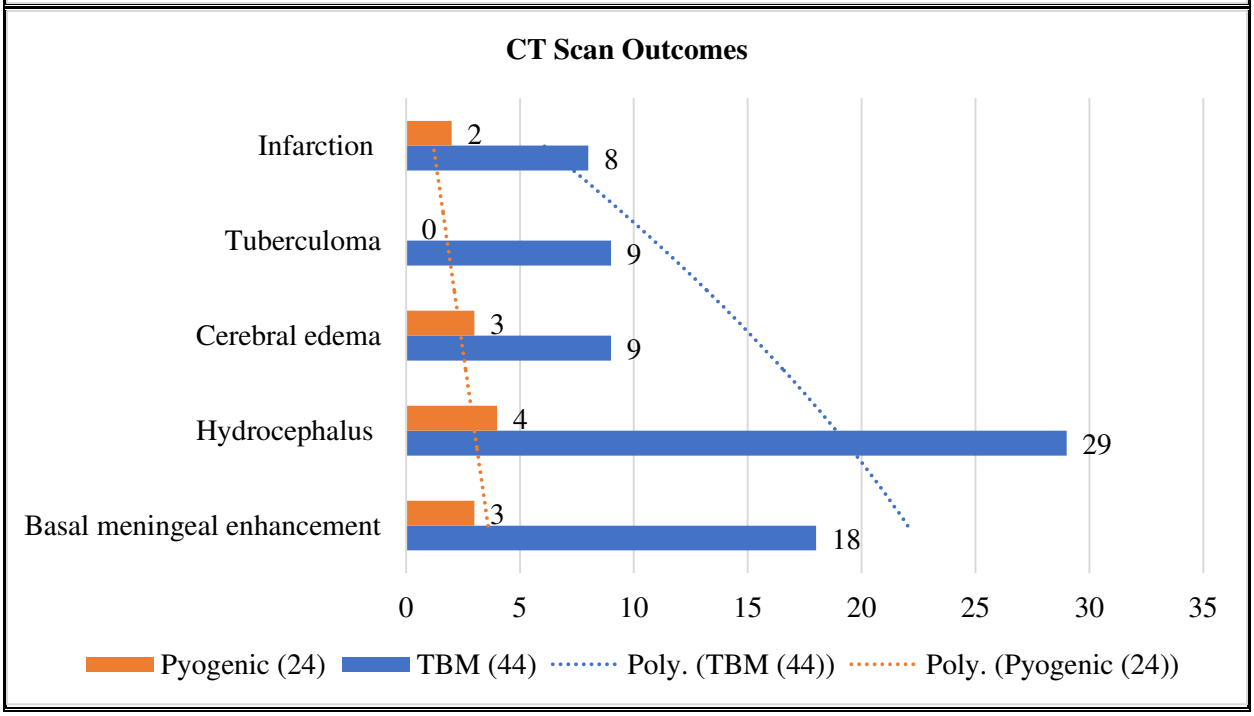
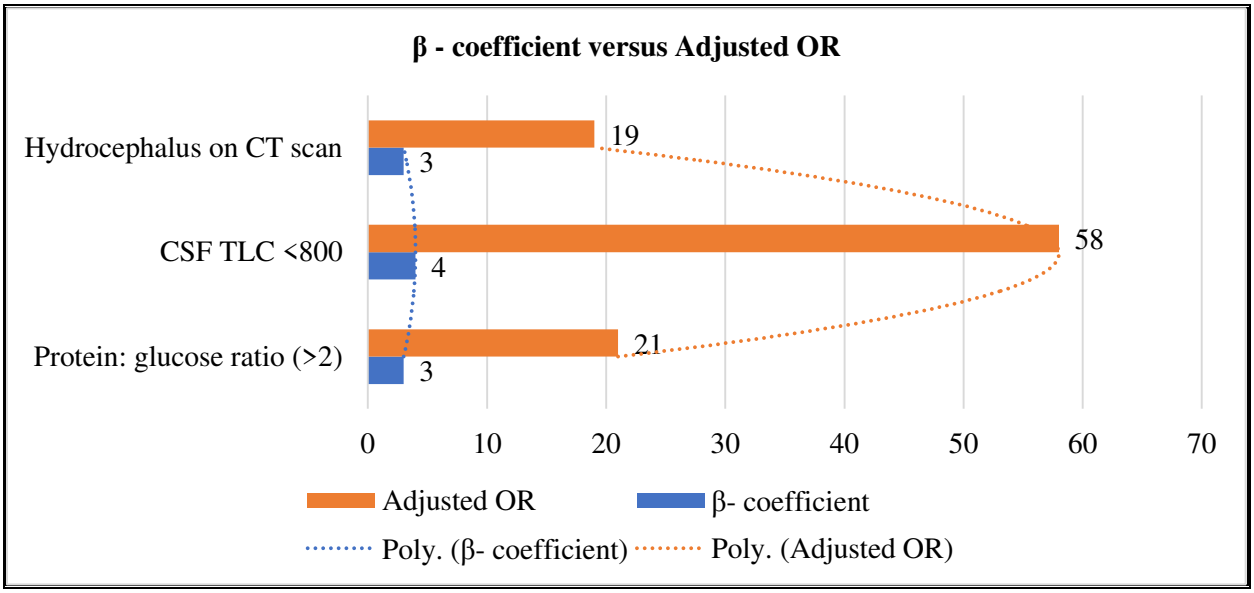

CT Scan Outcomes
Infarction
Tuberculoma
Cerebral edema
Hydrocephalus
Basal meningeal enhancement
2
8
0
9
3
9
4
29
3
18
0 5 10 15 20 25 30 35
Pyogenic (24)
TBM (44)
Poly. (TBM (44))
Poly. (Pyogenic (24))

Table – II: Multiple Logistic Regression Analysis

Clinical parameters	β - coefficient	Adjusted OR	95.0% C.I for Adjusted OR
Protein: glucose ratio (≥ 2)	3	21	4.7 – 93
CSF TLC less than 800	4	58	5 – 649
Hydrocephalus as on CT scan	3	19	3.3 – 109



A detailed laboratory and clinical parameters univariate analysis of pyogenic and TB meningitis and analysis of the multiple Logistic Regression has been shown in Table I & II.

DISCUSSION:

On an average back in 2009 a total of 139/100,000 cases of TB were reported having a death rate of 20/100000 [1]. Diagnostic and management is very much required for the TB cases as it is one of the growing healthcare issues faced by every part of the world. Delay may lead to severe outcomes which is primarily associated with the diagnostic of the laboratory and initiation of the intervention whether in the case of extrapulmonary or pulmonary TB [10]. The appropriate therapy can be initiated through probable an early TB diagnosis [5, 16].

CSF value glucose and protein are known to the numerous bacterial meningitis, which is rarely reported in the significant TBM cases [3, 15]. We analyzed in this retrospective research analysis a protein to glucose proportion in CSF; which can be stated as a proportion above 2 was significant because of moderately low level of the glucose and very high level of the protein as observed in the TBM cases; whereas, very low level of glucose and moderately high level of protein in bacterial meningitis patients. In the rigorous assessment of these evaluations held in the large-scale research studies we can imply it to the TBM scoring system in Mycobacterium TB absence on the culture of CSF (biochemical assessment of CSF is the routine pediatric meningitis cases healthcare facilities of secondary and tertiary levels).

TBM group was observed with a History of focal neurological signs and seizures, which as same as stated in the past studies [17]. No difference was attributed to the inflammatory markers like C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and total leukocyte count (TLC) in both the groups of the research. In the same way the CT scan was employed in those TBM cases which were associated with non-specific diagnostic yield [19]. However, few research studies have also reported the importance of hydrocephalus, basal enhancement, high density within basal cisterns as observed in the non-contrast CT scan, infarction and their value as a TBM diagnostic clue [20]. Hydrocephalus was

observed in 66 percent of TBM cases through CT scan which is comparable with other reports [21].

TBM is graded as one of the chronic disorders, the appearance of CSF is usually associated with the moderate leukocytes count and lymphocytes predominance. CSF cut-off value in the TBM diagnosis was noticed as (< 1000) in majority of the research outcomes [3, 5, 22]. We observed (< 800) CSF cell count which is a TBM predicator. Kenneth Jones Scoring Criteria (KJSC) is repeatedly utilized criteria designed back in 1960 [23]. KJSC requires an update in few of the features such as TST with low sensitivity inheritance and malnutrition. Moreover, as the human immune deficiency virus (HIV) has emerged, the set criteria may present low HIV infection sensitivity in the patients [24].

CONCLUSION:

We observed a set of simple laboratories, clinical and radiological criteria which can be helpful in the prediction of the TB meningitis. The cerebrospinal fluid value protein to glucose proportion requires validation in the large-scale research studies which can be confirmed through bacteriological TB meningitis case.

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