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Correlation between cerebrospinal fluid routine and microscopic examination with clinicopathological parameters in patients with meningitis

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ABSTRACT

Background: Cerebrospinal fluid examination is very useful and important in patients with neurological disease such as meningitis. CSF examination with quantification of polymorphs, lymphocytes and total count are the standard procedure in suspected case of infection. Our objective is to determine the correlation between clinicopathological parameters, routine and microscopic values. *Material and Method:* Total of 145 patient's reports included who were clinically suspected and underwent lumbar puncture from January 1st to 31st December 2021. *Result:* Meningitis was diagnosed in 82 male and 63 female patients over one year period. Fever was present in 99.3% patients with 65.5% experiencing headache, 56% vomiting with 68.9% experiencing neck stiffness and 73.1% had rash on the body. All symptoms showed significant p-value except headache when correlated with age group. Clinicopathological parameters significantly correlated with routine and microscopic values. *Conclusion:* CSF parameters are very useful as point of care tool for assessing patients with meningitis. Our study showed a very significant correlation between laboratories with clinicopathological parameters which can help clinicians for proper management of disease.

Keywords: Meningitis, Cerebrospinal fluid, Clinicopathological, Correlation, routine and Microscopic parameter

1. INTRODUCTION

The Cerebrospinal fluid (CSF) is clear body fluid that occupies the space between the arachnoid mater and the pia mater. It is formed in the choroid plexus through filtration and active transport. It protects the brain from the sudden change in stress and maintains stable chemical environment and removes wastes products (Egu and Ogunniyi 2020; Shah et al., 2020). Cerebrospinal fluid assessment is one of the most crucial aspects in laboratory diagnosis of meningitis. Analysis of the Cerebrospinal fluid abnormalities

caused by bacterial, mycobacterial, and fungal infections can greatly facilitate diagnosis and guide initial treatment (Alves et al., 2015; Landaas and Lippe, 2016; Mitra et al., 2018). The study aims to analyze of CSF examination in patients who are suspected for having meningitis and correlating routine and microscopic finding with clinicopathological parameters which might be helpful to guide and further management of the disease.

2. MATERIALS AND METHODS

Study area

The study was carried out at the Parul Sevashram Hospital, Vadodara. It is approximately 750 bedded tertiary medical facility located in Waghodia, Gujarat.

Study design and data collection

We retrospectively reviewed the laboratory records of all patients with suspected for meningitis who received lumbar punctures from 1st January 2021 to 31st December 2021. Clinical and Pathological data was retrieved from Medical Record Room and laboratory record books and Microsoft Excel spreadsheet. The study was approved by the Parul University Institutional Ethical Committee of Human Research (PU-IECHR) with approval number PUIECHR/PISMR/00/081734/4009.

Patient Selection

All the cases of meningitis at Parul Sevashram Hospital from 1st January 2021 to 31st December 2021; We reviewed in detail the records of those patients' case files which used to confirm information from other data sources (example pathology laboratory records).

Inclusion Criteria

Patient with clinical diagnosis of meningitis requiring lumbar puncture for confirmation of the diagnosis

Exclusion Criteria

Anybody diagnosed with some other neurological condition and not fit for lumbar puncture (presence of papilledema, lower platelet count).

Data Analysis

Statistical analysis was performed using Statistical Package for the Social Science Software, (SPSS) version 26.0. Cytological and Biochemistry parameters were compared with Age, Fever, Neck stiffness, Vomiting, Rash using one way anova. A statistical p-value <0.05 was consider statistically significant.

3. RESULTS

A total of 145 patients were enrolled in this study that underwent a lumbar puncture from 1st January 2021 to 31stDecember 2021. The study population had 82 Male (56.5%) and 63 Female (43.5%) patients. In relation to age wise distribution maximum specimen were received in 30 years to 60 years followed by 1 year to 14 years age group (Table 1). The physical examination of CSF sample (n=145) included the appearance, color and present of coagulum in CSF examination (Table 2).

Table 1 Age and Gender wise distribution of suspected cases of Meningitis

AGE GROUP	GENDER				TOTAL	
	MALE		FEMALE			
	N	%	N	%	N	%
>1	15	10.4	11	7.6	26	18
1 – 14	24	16.6	13	8.9	37	25.5
14-30	8	5.5	19	13.1	27	18.6
30 - 60	28	19.4	16	11	44	30.4
<60	7	4.8	4	2.7	11	7.5
Total	82	56.5	63	43.5	145	100

Table 2 Physical examination of Cerebrospinal fluid (CSF)

Physical Examination	Criteria	Number of Specimen
Appearance	Clear	125
	Hazy	18
	Hemorrhage	1
	Turbid	1
Color	Colorless	112
	Pale Yellow	21
	Mild Reddish	11
	Reddish	1
Coagulum	Present	1
	Absent	144

Age had statistically significant positive correlation with fever, vomiting, neck stiffness and rash (p = 0.009, 0.006, 0.011 and 0.07) and negative correlation with the presence of headaches (p = 0.0). Among the total processed specimen (n = 145) where 99.3% cases had fever and only 0.7% where asymptomatic. One way Anova test was applied in present study and yield a statistically significant correlation between presence of fever as a symptom and high total count (p = 0.001) and high percentage of Polymorphs (p = 0.014) in CSF examination. While there was positive correlation between presence of fever and increased percentage of lymphocytes in CSF but the correlation was not found statistically significant in study (p = 0.063) (Table 3).

Table 3 Fever compared with microscopic parameter

FEVER CORRELATED WITH TOTAL COUNT, POLYMORPHS AND LYMPHOCYTES						
Fever		Sum of Squares	df	Mean Square	F	Sig.
Total Count	Between Groups	1292965.463	1	1292965.463	16.981	.000
	Within Groups	10888497.889	143	76143.342		
	Total	12181463.352	144			
Polymorphs	Between Groups	5157.004	1	5157.004	6.239	.014
	Within Groups	117376.434	142	826.595		
	Total	122533.437	143			
Lymphocytes	Between Groups	4248.023	1	4248.023	3.518	.063
	Within Groups	172652.639	143	1207.361		
	Total	176900.662	144			

Headache (n = 145) where 65.5% patient represented headache and 9.0% were asymptomatic and 5.5 % patient complaint was not specified. We also found Headache had a statistically significant correlation with high percentage of polymorphs and high percentage of lymphocytes (p = 0.022 & p = 0.010). While there was positive correlation between presence of headaches and increased level of total counts in CSF, it was not statistically significant (p = 0.608) (Table 4).

Table 4 Headache compared with microscopic parameter

HEADACHES CORRELATED WITH TOTAL COUNT, POLYMORPHS AND LYMPHOYTES						
		Sum of Squares	df	Mean Square	F	Sig.
Total Count	Between Groups	85179.612	2	42589.806	.500	.608
	Within Groups	12096283.740	142	85185.097		
	Total	12181463.352	144			
Polymorphs	Between Groups	6491.284	2	3245.642	3.944	.022
	Within Groups	116042.154	141	822.994		
	Total	122533.437	143			
Lymphocytes	Between Groups	11023.548	2	5511.774	4.718	.010

	Within Groups	165877.114	142	1168.149		
	Total	176900.662	144			

Vomiting (n =145) where 56% patient represented vomiting as complaint, 33% patient where asymptomatic and 9.7 % complaints were not specified. When we applied a correlation between presence of vomiting with increased Total count and high percentage of Polymorphs in study where there was statistically significant was established between presence of vomiting and increased total counts (p = 0.012) and high percentage of polymorphs (p = 0.041), but presence of vomiting with increased lymphocytes percentage (p = 0.510) was not found statistically significant in present study (Table 5).

Table 5 Vomiting compared with microscopic parameter

VOMITING CORRELATED WITH TOTAL COUNT, POLYMORPHS AND LYMPHOYTES						
		Sum of Squares	df	Mean Square	F	Sig.
Total Count	Between Groups	741867.480	2	370933.740	4.604	.012
	Within Groups	11439595.871	142	80560.534		
	Total	12181463.352	144			
Polymorphs	Between Groups	5437.491	2	2718.746	3.274	.041
	Within Groups	117095.946	141	830.468		
	Total	122533.438	143			
Lymphocytes	Between Groups	1670.683	2	835.341	.677	.510
	Within Groups	175229.979	142	1234.014		
	Total	176900.662	144			

Neck Stiffness (n = 145) where 68.9% patient represented complaint 31.1% patients where asymptomatic. The study shows that there was statistically significant with presence of neck stiffness with increased percentage of polymorphs (p = 0.006) and increased percentage of lymphocyte (p = 0.017), But there was positive correlation between presence of neck stiffness with high total count in CSF but correlation was not statistically significant (p = 0.074) (Table 6).

Table 6 Neck Stiffness compared with microscopic parameter

NECK STIFFNESS CORRELATED WITH TOTAL COUNT, POLYMORPHS AND LYMPHOYTES						
		Sum of Squares	df	Mean Square	F	Sig.
Total Count	Between Groups	270126.702	1	270126.702	3.243	.074
	Within Groups	11911336.650	143	83296.060		
	Total	12181463.352	144			
Polymorphs	Between Groups	6334.456	1	6334.456	7.741	.006
	Within Groups	116198.982	142	818.303		
	Total	122533.438	143			
Lymphocytes	Between Groups	6891.171	1	6891.171	5.796	.017
	Within Groups	170009.491	143	1188.878		
	Total	176900.662	144			

Rash (n = 145) in which 73.1% patient represented complaint for rash and 26.9% were asymptomatic patients. There was no correlation between presence of rash and increased total count where statistically significant was not established between them (p = 0.99) and presence of rash with increased percentage of polymorphs (p = 0.21) and increased lymphocytes (p = 0.250) was also statistically not significant (Table 7 and Fig 1).

Table 7 Rash compared with microscopic parameter

RASH CORRELATED WITH TOTAL COUNT, POLYMORPHS AND LYMPHOYTES						
		Sum of Squares	df	Mean Square	F	Sig.
Total Count	Between Groups	230912.690	1	230912.690	2.763	.099
	Within Groups	11950550.662	143	83570.284		
	Total	12181463.352	144			
Polymorphs	Between Groups	4508.440	1	4508.440	5.424	.021
	Within Groups	118024.998	142	831.162		
	Total	122533.438	143			
Lymphocytes	Between Groups	1634.683	1	1634.683	1.334	.250
	Within Groups	175265.979	143	1225.636		
	Total	176900.662	144			

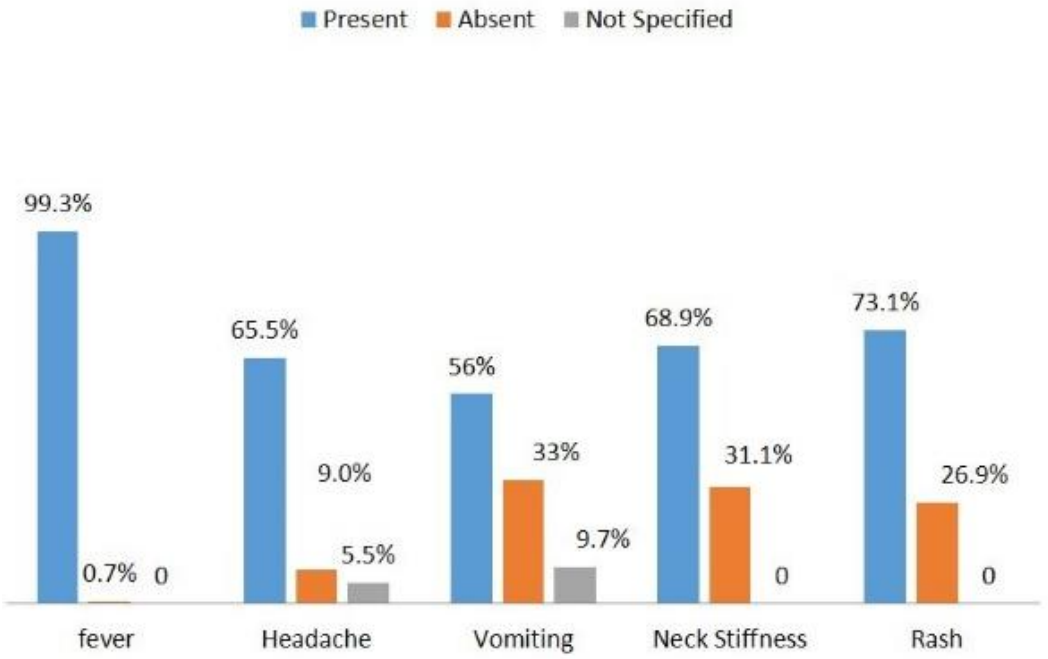

Figure 1 Frequency (%) of symptoms of meningitis

Routine Biochemistry

When we correlate fever with protein, sugar and Adenosine Deaminase (ADA), there was no statistically significant correlation was established between them (p = 0.493, 0.720, 0.697), (Table 8) but there was statistically significant correlation between headache and ADA (p = 0.031) while there was positive correlation but protein and sugar with headaches but it was not found statistically significant (p = 0.906, 0.990) (Table 9). It also, suggested that there was presence of correlation between vomiting and protein and sugar where there was significant correlation established between presence of vomiting and protein (p= 0.025).

Table 8 Fever compared with routine parameter

FEVER						
		Sum of Squares	Df	Mean Square	F	Sig.
Protein	Between Groups	1159.367	1	1159.367	.472	.493
	Within Groups	351294.441	143	2456.604		
	Total	352453.808	144			

Sugar	Between Groups	234.506	1	234.506	.129	.720
	Within Groups	260173.660	143	1819.396		
	Total	260408.166	144			
ADA	Between Groups	32.180	1	32.180	.152	.697
	Within Groups	30303.262	143	211.911		
	Total	30335.441	144			

Table 9 Headache compared with routine parameter

HEADACHE						
		Sum of Squares	Df	Mean Square	F	Sig.
Protein	Between Groups	490.899	2	245.449	.099	.906
	Within Groups	351962.909	142	2478.612		
	Total	352453.808	144			
Sugar	Between Groups	35.667	2	17.833	.010	.990
	Within Groups	260372.499	142	1833.609		
	Total	260408.166	144			
ADA	Between Groups	1443.198	2	721.599	3.547	.031
	Within Groups	28892.244	142	203.467		
	Total	30335.441	144			

In CSF presence of vomiting and sugar was statistically significant (p = 0.001) where there was positive correlation between presence of vomiting with ADA in CSF but the correlation was not found statistically significant (p = 0.920) (Table 10). There was positive correlation between presence of neck stiffness with protein sugar ADA in CSF but the correlation was not found statistically significant (p = 0.60, p = 0.512, p =0.067) (Table 11).

Table 10 Vomiting compared with routine parameter

VOMITING						
		Sum of Squares	Df	Mean Square	F	Sig.
Protein	Between Groups	17921.212	2	8960.606	3.804	.025
	Within Groups	334532.596	142	2355.863		
	Total	352453.808	144			
Sugar	Between Groups	26494.134	2	13247.067	8.042	.000
	Within Groups	233914.032	142	1647.282		
	Total	260408.166	144			
ADA	Between Groups	35.473	2	17.737	.083	.920
	Within Groups	30299.968	142	213.380		
	Total	30335.441	144			

Table 11 Neck Stiffness compared with routine parameter

NECK STIFFNESS						
		Sum of Squares	Df	Mean Square	F	Sig.
Protein	Between Groups	8638.263	1	8638.263	3.593	.060
	Within Groups	343815.545	143	2404.305		
	Total	352453.808	144			

Sugar	Between Groups	784.745	1	784.745	.432	.512
	Within Groups	259623.421	143	1815.548		
	Total	260408.166	144			
ADA	Between Groups	705.392	1	705.392	3.404	.067
	Within Groups	29630.049	143	207.203		
	Total	30335.441	144			

The study show that there was correlation between presence of rash and protein was statistically significant (p = 0.003) while there was positive correlation between presence of Rash with Sugar and ADA in CSF but the correlation was not found statistically significant in present study (p = 0.683 and p = 0.215) (Table 12).

Table 12 Rash compared with routine parameter

RASH						
		Sum of Squares	df	Mean Square	F	Sig.
Protein	Between Groups	21432.338	1	21432.338	9.259	.003
	Within Groups	331021.470	143	2314.835		
	Total	352453.808	144			
Sugar	Between Groups	304.453	1	304.453	.167	.683
	Within Groups	260103.713	143	1818.907		
	Total	260408.166	144			
ADA	Between Groups	325.755	1	325.755	1.552	.215
	Within Groups	30009.686	143	209.858		
	Total	30335.441	144			

Routine and Microscopic

There was positive correlation between high polymorphs in CSF and high protein which was statically significant (p= 0.005) while negative correlation was found between percentage of polymorphs and value of total sugar (p= 0.00). Where there was statically significant correlation was established between value of ADA and percentage of polymorphs and lymphocytes in CSF (p= 0.00). We also found that whenever value of protein was high, there was less percentage of polymorphs (p = 0.02) there was lesser percentage of lymphocytes similarly; sugar value was not statically significant, and hence correlation was established only between percentage of lymphocytes and value of sugar in CSF (Table 13).

Table 13 Microscopic parameters compared with routine parameter

DONE PAIRED SAMPLES TEST									
		Paired Differences					T	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Total Count - Protein	29.90952	285.44097	23.70458	-16.94437	76.76340	1.262	144	.209
Pair 2	Total Count - Sugar	21.5807	302.1241	25.0900	-28.0117	71.1730	.860	144	.391
Pair 3	Total Count - ADA	87.1883	291.0708	24.1721	39.4103	134.9663	3.607	144	.000

Pair 4	Polymorphs - Protein	-44.40361	51.44165	4.28680	-52.87730	-35.92992	-10.358	143	.000
Pair 5	Polymorphs - Sugar	-52.6028	54.5577	4.5465	-61.5898	-43.6158	-11.570	143	.000
Pair 6	Lymphocytes - ADA	69.2986	38.3156	3.1819	63.0093	75.5880	21.779	144	.000
Pair 7	Lymphocytes - Protein	12.01986	62.38151	5.18050	1.78021	22.25951	2.320	144	.022
Pair 8	Sugar - Lymphocytes	-3.6910	52.4275	4.3539	-12.2968	4.9147	-848	144	.398
Pair 9	ADA - Polymorphs	-13.0229	31.0484	2.5874	-18.1373	-7.9085	-5.033	144	.000

4. DISCUSSION

CSF is a transparent fluid that circulates throughout the brain and spinal cord. The composition of CSF remains consistent under normal circumstances (Finsterer et al., 2009; Pandey et al., 2015). The color, appearance, composition, total count and differential count can be altered in various neurological conditions especially in acute situation (Dunbar et al., 1998; Shah et al., 2020). Diagnosis of meningitis is done by various CSF composition using laboratory parameters. Meningitis is a medical emergency which need an early diagnosis and aggressive therapy (Conly and Ronald, 1983). This study gives us an overview of the meningitis diseases. In different age group from 2020 to 2021 we have included all types of meningitis in this study rather than just bacterial, viral or fungal meningitis. We have reviewed the published result from randomized controlled, cross sectional or observation studies. The result of the study may be useful in guiding and managing infection.

Physical examination of CSF should be done as soon as the sample is collected. It includes parameters like color which is a crucial diagnosis characteristic of CSF, it should be done within 30 min of collection because after that RBC start to lysis which can affect the result. Normally CSF is colorless and transparent like distil water and does not clot. In any abnormal cases color of CSF changes in straw, pink, yellow or amber pigments which indicates the presence of hemoglobin, RBC, bilirubin or increased protein (Hrishi and Sethuraman, 2019; Laving et al., 2003; Schmidt et al., 2006).

In this study protein level were greater than normal value (226.8 mg/dl) and glucoses were lower than normal range but in some cases of meningitis we found that glucose level were normal (40 - 80 mg/dl) (Schmidt et al., 2006). Markedly decreased CSF glucose with markedly increased total protein and decreased in CSF glucose with markedly increased in total protein, high total count. Similarly, study also mention that the examination of CSF of a patient with acute bacterial meningitis characteristically reveals a cloudy fluid and increased in total counts and predominance of polymorphs and lymphocytes, a low glucose concentration and raised protein value (Chadwick and Lever, 2002; Lamonte et al., 1995; Mitra et al., 2018; Pandey et al., 2015). Due to the infection the protein level rises and thus changes in protein value help in distinguish between viral and bacterial meningitis. Among the fungal meningitis, protein level was slightly increased and glucose was within normal range. These finding are in accordance with other researchers (Alves et al., 2015; Domingues et al., 2019; Dunbar et al., 1998; Mitra et al., 2018).

In our study, we found that fever (99%) was common symptoms among all the patients which we processed. Similar findings were found in (Aminzadeh and Roudgari, 2010; Brouwer et al., 2010; Garges et al., 2006; Laving et al., 2003) published paper in which they mention that fever is an universal symptoms in patients suffering from meningitis. We also found that rash (73%), Headache (65%), neck stiffness (63%), Vomiting (56%) was present among the patients which can be useful for ruling out the meningitis. Similar finding were also found other study (Ghia and Rambhad, 2021; Lamonte et al., 1995; Philip et al., 2015).

The study has some limitations, it is local study of PSH. It is retrospective design allow us only to analyze the CSF exams and patient's records. Despite we believe that the results are relevant and clinically important especially in this sample compared to published studies. Furthermore, we would require data in large scale from multicenter and prospective studies to find the greater utility in predicting meningitis.

5. CONCLUSION

In patients with acute neurological disorder, CSF analysis is very important parameter for diagnosis, prognosis and evaluation of various types of meningitis. Clinicopathological parameters are useful parameters as point of care tool for assessing patients with meningitis. Our study showed a very significant correlation between laboratories with clinicopathological parameters which can

help clinician to enquire proper management of disease. These data showed the importance of studies that can be clarifying the changes in routine and microscopic correlation between clinicopathological parameters in CSF.

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Author's Contribution

Swapnilraj Prajapti is the primary author and has contributed to the data collection, compilation and analysis. Dr. Akshay Panchal and Ankita Priyadarshini contributed to the conceptualisation and design of the study. Swapnilraj Prajapti and Dr. Akshay Panchal contributed to the interpretation of the results and drafting of manuscript. Dr. Akshay Panchal and Ankita Priyadarshini contributed to the proof reading and final review of the article to be published.

Ethical Approval

The study was approved by the Parul University Institutional Ethics Committee for Human Research (PU-IECHR) with approval number: PUIECHR/PIMSR/00/081734/4009 presented in 40th meeting.

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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