P- ISSN 1991-8941 E-ISSN 2706-6703 *Journal of University of Anbar for Pure Science (JUAPS)* Open Access
2009,(3), (3) :01-05

The Role of Lactate Dehydrogenase in Differentiating Between Bacterial and Non -Bacterial Meningitis in children Under Five Years in Ramadi Maternity and Children Hospital

Saleem O. Qateae * , Muhammad M. Mushrif ** , Adnan M Jasim ***

* Ministry of health – Al-Anbar general health directorate
** college of medicine –university of al- Anbar
***college of medicine – university of Al- Anbar

ARTICLE INFO

Received: 19 / 5 /2022
Accepted: 28 / 5 /2022
Available online: 14/6/2012
DOI: 10.37652/juaps.2009.15592

Keywords:
Lactate Dehydrogenase ,
Meningitis ,
Ramadi.

ABSTRACT

The present study was designed to find out the usefulness of lactate dehydrogenase (LDH) level in cerebrospinal fluid (CSF) in differentiating bacterial from non-bacterial meningitis in children below 5 year of age. A total of 177 patients who were admitted to the AL-Ramadi Maternity and children hospital, AL-Anbar, Iraq During a period of one year (from 1st.November / 2007 to 1st.November 2008), for diagnosis and treatment of meningitis were included in the study. Cerebrospinal fluid samples were collected from patients by lumbar puncture (LP) for diagnosis. Levels of LDH were measured spectrophotometrically in Randox commercially prepared kits and compared in bacterial, non-bacterial meningitis and controls.The study revealed that only 24 cases have meningitis. Bacterial meningitis present in 19(79%) . Of them 11(46%) with positive culture and 8(33%) with negative culture (partially treated), while the remaining 5(21%) were found to be non-bacterial cases. The study concluded that measurement of LDH levels in CSF is beneficial in differentiating bacterial from non-bacterial meningitis since it was significantly increased in bacterial meningitis.

Introduction:

Meningitis is an inflammation of the arachnoid, piamater ,and the intervening cerebrospinal fluid .1. It can becaused by variety of infectious agents, bacterial meningitis is a significant cause of morbidity and mortality, especially in pediatric population.2. Meningitis also can caused by viral, fungi, chemical irritation, drug allergies and tumors.3,4

The incidence of meningitis during the first year of life is 20 times higher than in older children and adults.5

Diagnosis of meningitis can be achieved by clinical examination and laboratory finding of cerebrospinal fluid (CSF) which is obtained through lumbar puncture (L.P) for cell count and differential, sugar and protein ,culture of CSF ,direct microscopy for gram stain study, Ziehl–Nelson staining for T.B meningitis, immune diagnosis of meningitis are Enzyme-Liked Immunosorbant Assay (ELISA) counterimmuno - electrophoresis, polymerase chain reaction (PCR) , latex agglutination test (LAT), and general laboratory tests which include blood count ,blood sugar, C-Reactive protein and blood culture.6,7,8

Lactate deyhydrogenase, a tetramer protein comprised of four monomer, is expressed as five isoenzymes having different distribution in various tissues. Brain tissue which is dependent in aerobic metabolism has a predominance of the aerobically active LDH1and LDH2 isoenzymes .9,10

Lactate dehydrogenase is intracellular enzyme, it is sensitive indicator of bacterial meningitis.11,12 . It is more sensitive as early indicator of bacterial meningitis than is glucose, and appear to help to differentiate bacterial from non-bacterial meningitis.13,14

The main objective of the present study was to estimate lactate dehydrogenase levels in CSF sample from patients under 5 years age with meningitis and evaluate the benefit of this important enzyme in differential diagnosis of meningitis.

* Corresponding author at: Ministry of health – Al-Anbar general health directorate,

Experimental:-

A prospective hospital based study was done during a period of one year (from 1st.November / 2007 to 1st.November 2008). All patients from one month to 5 years admitted to the AL-Ramadi maternity and children hospital in Al-anbar governorate, Iraq with a presumptive diagnosis of meningitis were included in the study.

2-5 ml of CSF which had been collected by L.P were sent directly to the hospital laboratory to be studied for cell count and differential, protein, sugar, lactate dehydrogenase level , gram stain, and culture.

The level of LDH was considered as high when it is more than 22 U/l 15Levels of LDH in CSF were estimated using a colorimetric method in a commercially prepared kits produced by Randox _UK company.

Data were analyzed statistically using SPSS version 10. P value less than 0.05 was considered significant. Validity of the test was calculated according to its sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

Results

A total of 24 cases were regarded as meningitis with CSF cells more than 5. Cerebrospinal fluid culture for meningitis were positive in 11 (46%), while 8 (33%) cases had negative results which considered as partially treated and the remaining 5(21%) regarded as non bacterial meningitis. Eight patients(33.3%) of meningitis cases were received antibiotic before admission to the hospital. Twenty-four samples that were found to be clear (non meningitic) were used as controls.

Patients were grouped according to age into three groups (1month to 1year, 1 year to 3 years, and 3-5 years). The highest number and percentage of meningitis patients were noticed in first age group (1 month to 1 year) which represent 11(45.8%), followed by the second age group 10(41.7%) ,while only 3 patients of cases were recorded in the third age group (Table 1).

Table1: Distribution of results of meningitis according to type and age:

Age group	Bacterial No.(%)	Non_ Bacterial No.(%)	Total
1 month_1year	9(82%)	2(18%)	11(45.8%)
>1 _3 years	9 (90%)	1(10%)	10(41.7%)
> 3_5 years	1 (25%)	2(75%)	3(12.5%)
Total	19 (79%)	5(21%)	24(100%)

Comparison between different age groups in distributions is not significant (P value >0.05).

Males were found to be more affected than females in a ratio of 1.66:1 which is statically not significant (P Value>0.05) . (Table 2).

Table2:Results of cases of meningitis and controls according to gender:

Gender	Patients No(%)	Controls No(%)
male	15(62.5)	15(62.5)
female	9(37.5)	19(37.5)
Total	24(100)	24(100)

Comparison between 2 genders is not significant (P value >0.05)

The mean levels of CSF-LDH enzyme were found to be relatively high in cases of bacterial meningitis in all age groups while it was almost equal in non bacterial meningitis and controls .Table(3).

Table 3 : Mean levels of CSF-LDH (U/L) in patients and controls according to age groups :

Cases	1month-1year ×±sd	1year-3years ×±sd	3years-5years ×±sd	Total number
Bacterial meningitis	58±1	57±4	62	19
Non bacterial meningitis	23±1	24	24±3	5
controls	21±1	20±2	22±1	24

Comparison between bacterial and non-bacterial, and bacterial and controls was significant (P value =0.001) .while comparison between non bacterial and controls was not significant (P value >0.05)

Depending a cutoff point of 22 IU/L , the % sensitivity , % specificity , % Positive Predictive Value , % Negative Predictive Value , and % Accuracy of the test were found to be 89.4 ,80 ,94.4 , 66.6 , and 87.5 respectively .

Discussion:

Meningitis is still a very common and serious disease that may lead to death and many of those who survive may be left disabled .the final outcome depends on considerable degree of early diagnosis and appropriate treatment.

The routine examination of CSF for cell count, glucose, and protein when meningitis is suspected, along with use of gram's stain and bacterial culture, are all valuable in differential diagnosis of meningitis 13

The present study included 177 CSF samples from patient admitted to the maternity and childhood hospital in Ramadi city with a presumptive clinical diagnosis of meningitis. Of them 24 patients were proved to be meningitis cases. 19(79%) of them have bacterial meningitis 11(46%) with positive culture and 8(33%) with negative culture (partially treated), while the remaining 5(21%) were found to be non-bacterial cases, similar results were reported as bacterial meningitis and non-bacterial meningitis in Saudi (68%,32%)21and Yemen(74%,26%)16 .

Thirty three percent of meningitis cases had received antibiotics before admission to hospital which is the probable cause to give negative CSF culture. Similar observations were reported in United State of America (10%) 17, United Kingdom (18%)18, and Iraq (14.3)19

In the present study , the highest number of patient with meningitis was noticed in the first age group (1month_1 year) (45.8%), which was more than other age groups but the difference was statically not significant (P. value > 0.05), these findings are in agreement with many reports from Palestine 20 (46.6%), oman21(48.2%), and Libya22(49.4%).

The incidence of bacterial meningitis is higher in developing countries than developed countries and particularly high in children under one year of age. 23,24,25,26 The possible causes are immaturity of the immune system , and the lack in the pre –exposure of the body to these organisms , which enhance the memory of the immune system to fight against these invaders 27,28

According to sex ,we found that males were more affected than females in ratio 1.66:1 , but the difference was statically not significant (P. value > 0.05), similar results were reported by some investigator 29, 30. The little predominance of male patient in meningitis could be attributed to many factors e.g. the outside home contacts which is more in males than females , and the exposure of males to many factors from community like active or passive exposure to cigarette smoking

The % sensitivity , % specificity , % Positive Predictive Value , % Negative Predictive Value , and % Accuracy of the test were found to be 89.4 ,80 ,94.4 , 66.6 , and 87.5 respectively. These findings are supported by many reports 31 , 32, 33 , 34 .however , high index of suspension of meningitis and rapid diagnosis is essential for favorable results ,thus the test under study is easy and rapid and can be done rottenly in all hospital laboratories and it will prevent the delay in diagnosis which may increase morbidity and mortality due to this important disease .

In the present study , the usefulness of CSF-LDH is in differentiating between bacterial and non bacterial meningitis (P. value < 0.05) is comparable with other researches 35,36,37 , However, some investigators reported that LDH -CSF may not be useful in differentiation between septic and aseptic meningitis but it may act as a corroborative evidence of meningitis. 38,39,40.however , it is a rapid ,relatively sensitive , specific , and easily performed test and helpful in differentiating bacterial from non bacterial meningitis. it is recommended to be used in the laboratory procedures beside conventional methods . Further future studies are recommended on the analysis of LDH isoenzymes pattern in CSF and serum to determine the benefit of LDH sub fractions (LDH1, LDH2, LDH3, LDH4, LDH5) in differential diagnosis of meningitis.

References

1. Swartz M.N. Bacterial meningitis in: Cecil textbook of Medicine 21st EdGoldman and Bennett. W.B. Saunders Company: 1644 – 1649.
2. Dawson K.G., Emerson J.C., Burns J.L. Fifteen years of experience with bacterial meningitis. Pediatric. Infect. Dis. J. 18(9) :816 - 822 .
3. Wenger JD , Hightower AD , Facklam RR , Gaventa S , et al. the Bacterial meningitis study group ; Bacterial meningitis in the , United states , 1986 : report of a multistate surveillance study . Journal of infectious diseases (1990) 162;1316 – 1323.
4. Types and causes of meningitis, meningitis research foundation office, England and Wales 2007.
5. Amir Vokshoor Viral meningitis: Article by MD, Staff, Department of neurosurgery, Woodland Hills, medical Center, January 9, 2004.
6. Bonadio WA. The cerebrospinal fluid: physiologic aspect and alteration associated with bacterial meningitis. Pediatr infect Dis J 1992; 11:423-32.
7. Colle J.G., Duguid J.P.; Fraser A.G.; Marmion B.P, et al. laboratory Strategy in the diagnosis of

infective syndromes. Churchill & Livingstone,14:35-94.

8. Charles G. Prober. Central nervous system infection .Nelson textbook of pediatrics, Kliegman, Behrman, Jenson, Stanton. Philadelphia18th edition 2007:2513.
9- Fleisher M, Wasserstrom WR,Schold SC, Schwartz MK, posner JB.Lactic dehydrogenase isoenzymes in the cerebrospinal fluid of patients with systemic cancer. Cancer 1981;47:2654-9.
10- Subhash MN, Rao BSS, Shankar SK. Changes in lactate dehydrogenase isoenzymes pattern in patients with tumors of the central nevous system. Neurochem Int 1993;22:121-4.
11. McArthur JC, Nance-Sproson te, Griffin de, et al. The diagnosis utility of elevation in cerebrospinal fluid beta 2-microglobulin in HIV-1 dementia.Neurology 1992;42:1707-12 .
12. Watson MA, Scott MG.Clinical utility of biochemical analysis of cerebrospinal fluid. Clin Chem1995;343-60.
13. J. A. Knight, S. M. Dudek, and R. E. Haymon Early (Chemical) Diagnosis ofBacterial Meningitis. Cerebrospinal Fluid Glucose, Lactate, and Lactate Dehydrogenase Compared. clin . Chem. 27(8): 1431-1434(1981).
14. Andreas Wellmer, Juliane Prange, Joachim Gerber, Gregor Zysk, et al. D-and L-lactate in Rabbit and Human Bacterial meningitis. Scandinavian Journal of infectious Diseases December 2001;33:909-913.
15-Coupal L, Suissa S, Szentveri T, Falutz J, et al .The clinical utility of serum lactate dehydrogenase in diagnosing pneumocystis carinii pneumonia among hospitalized AIDS patients.Clin invest med. 1992;15(4): 309-17.
16- Abdul Khaliq A. Sallam, Etilogy and presentation of Acute bacterial Meningitis in children at Al-Thawrah hospital, sanaa, yemen.
17- Converse, G. M., Gwalteny, j. M., Strassburg, D.A., and Hendley, j. O. (1973). Alteration of cerebrospinal fluid finding by partial treatment of bacterial meningitis. Journal of pediatrics, 83,220.
18- Jarvis, C. W., and Saxena, K. M. (1972). Does prior antibiotic treatment hamper the diagnosis of acute bacterial meningitis .An analysis of a series of 135 childhood cases. Clinical pediatrics, 11, 201.
19 – Al-Mawla S.O.G. A Study on the aetiology of bacterial meningitis and pre purposes.PhD Thesis. Al-Mustensiriyah University, College of Medicine 2002: P 51.
20- Izidore S. Losses, M .D.,cerebrospinal fluid lactate dehydrogenase isoenzyme Analysis for the,Hadassah university hospital December 1999;52:198.
21- Koul R.L.; Chacko A.(1994). Pattern of childhood meningitis in Oman. Saudi. Med. J. 19(4): 432-436.
22- Rao B.N.; Kashbur I.M.; Shembesh N.M. and El-Bargathy S.M. (1998). Aetiology and occurrence of a in Benghazi, Labyan Arab Jamahiriyia. East. Meditterr. Health.J.4 (1): 50-57.
23- Murray CJ and Lopez AD. Global Burden of Disease and Injury Series Vol II. Global Health Statistics. Geneva, 1996:285.
24- Baraff LJ,Lee SI and Schriger DL. Outcomes of bacterial meningitis in children: a meta-analysis. Pediatr Infect Dis J 1993; 12:389-94.
25- Quagliarello VJ, Scheld WM. Treatment of bacterial meningitis. N Engl J Med. 1997;336: 708 -16.
26- Al-Aun M.; Saleh F.; Ajlouni M.B.; Hazza I, et al. Bacterial Meningitis in children. J. Roy.Med. Serv 1994;1(2): 23-25.
27- Mayo Foundation for Medical Education and Research by Mayo Clinic Staff, infectious disease, meningitis; 11, 2007
28- Schuchat A., Wenger J. Epidemiology of bacterial meningitis. Annual Nestle 1997;55: 79-91.
29- Gastrin, B., Briem, H., and Rombo, Rapid diagnosis of meningitis with use of selected clinical data and gas-liquid chromatographic determination of lactate concentration in cerebrospinal fluid. J. Infect.Dis. (1979); 139:529-533 .
30- William Neches M.D.and Martin PlattM.D. cerebrospinal fluid LDH in 287 children, including 53 cases of meningitis of bacterial and non-bacterial etiology. Pediatrics1986;41(6):1097-1103.
31- W. E. Feldman, hillock. cerebrospinal fluid LDH activity. Clin pediatric 1978;17:372-375.
32- Krogsgaard AR,Ouaade. Glutamic acid oxaloacetic acid system. Acta Neurol Scand 1963;39:154-60.
33- Nussinovitch M, Klinger G, Magazanik A, Volovitz B, et al. increase creatine kinase brain isoenzyme concentration in cerebrospinal fluid with meningitis. Clin pediatr(phila)1996;35:349-51.

34- AKimor GA, Zinccheno VA, Sytinsky IA, palagnta VD. The gamma glutamyl transferase activity in hemorrhagic and ischemic stroke. Sov Med 1985;1:3-5 .
35- pagana, Kathleen Deska. Mosby's Manual of diagnostic and laboratory Tests. St Louis: mosby, inc.,1998.
36- Connolly K, Hammer SM. The acute aseptic meningitis syndrome. Infect Dis Clin North Am 1990;4:599-622.
37- Nelson S, Sealy DP, Schneider EF. The acute aseptic meningitis syndrome. Am Fam Physician 1993;48:809-15.
38- B. S. Nayak and Rama Bahat. Cerebrospinal fluidlactate dehydrogenase and glutamine in meningitis. Department of Biochemistry and medicine kasturba medical college 2005; 49(1):108-110.
39- Beaty HN,Oppenheimer S;Cerebrospinal fluid lactic dehydrogenase and its isoenzymes in infection of the central nerveous system. New Eng J Med 1988;279:1197-1202.
40- Khanna SK, Gupta DK, Gupta BK, Khanna P: Cerebrospinal fluid lactic dehydrogenase activity in various neurological disorders J Assooc phys Ind 1976;24:29-36.

دور انزيم اللاكتيت ديهايدروجينيز في التشخيص التفريقي بين التهاب السحايا الجرثومي وغير الجرثومي في الأطفال تحت سن الخامسة في مستشفى النسائية والأطفال في الرمادي

سليم عبيد كاطع ، محمد ماهر مشرف ، عدنان محمد جاسم

الخلاصة

صممت الدراسة الحالية بهدف معرفة أهمية تركيز إنزيم اللاكتيت ديهايدروجينيزفي السائل المخي ألشوكي في التفريق بين التهاب السحايا الجرثومي وغير الجرثومي في الأطفال تحت خمس سنوات في مستشفى النسائية والأطفال في الرمادي .شملت الدراسة ١٧٧ طفلا دون سن الخامسة من العمر يعانون من أعراض وعلامات التهاب السحايا وادخلو إلى المستشفى لغرض التشخيص والعلاج للفترة من ١ تشرين الثاني ٢٠٠٧ إلى١ تشرين الثاني ٢٠٠٨ حيث تم جمع السائل المخي الشوكي من هؤلاء الأطفال بطريقة البزل القطني لغرض التشخيص كما تم قياس تركيز إنزيم اللاكتيت ديهاديدروجينيز بطريقة المطياف الضوئي.من خلال الطرق المختبرية المتعددة للتشخيص ،تبين أن ٢٤ حالة يعانون فعلا من التهاب السحايا .بينت النتائج أن ١٩ حالة (٧٩%) يعانون من التهاب االسحايا البكتيري وينقسمون إلى ١١حالة (٤٦%) كانت نتيجة الزرع البكتيري موجبة وأن ٨ حالات (٣٣%) كانت نتيجة الزرع البكتيري سالبة بينما عُد العدد المتبقي ٥ حالات (٢١%) هو التهاب سحايا غير بكتيري.استنتجت الدراسة أن بالإمكان الاستفادة من قياس تركيز إنزيم اللاكتيت ديهايدروجينيز في السائل المخي ألشوكي للتفريق بين نوعي التهاب السحايا إذ انه يرتفع معنويا في حالة التهاب السحايا البكتيري.