

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

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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.

Key words : Lactate Dehydrogenase , Meningitis , Ramadi

Introduction:

Meningitis is an inflammation of the arachnoid, pia mater, and the intervening cerebrospinal fluid .1. It can be caused by variety of infectious agents, bacterial meningitis is a significant cause of morbidity and mortality ,especially in pediatric population.2. Meningitis also can be 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 dehydrogenase, 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 LDH1 and 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.

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 15 Levels 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)

are supported by many reports 31, 32, 33, 34. However, high index of suspicion of meningitis and rapid diagnosis is essential for favorable results, thus the test under study is easy and rapid and can be done routinely 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.

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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%) 21 and 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 (1 month_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%), Oman 21 (48.2%), and Libya 22 (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

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

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الخلاصة

صممت الدراسة الحالية بهدف معرفة أهمية تركيز إنزيم اللاكتيت ديهيدروجينيز في السائل المخي الشوكي في التفريق بين التهاب السحايا الجرثومي وغير الجرثومي في الأطفال تحت خمس سنوات في مستشفى النسائية والأطفال في الرمادي. شملت الدراسة 177 طفلاً دون سن الخامسة من العمر يعانون من أعراض وعلامات التهاب السحايا ودخلوا إلى المستشفى لغرض التشخيص والعلاج للفترة من 1 تشرين الثاني 2007 إلى 1 تشرين الثاني 2008 حيث تم جمع السائل المخي الشوكي من هؤلاء الأطفال بطريقة البزل القطني لغرض التشخيص كما تم قياس تركيز إنزيم اللاكتيت ديهيدروجينيز بطريقة المطياف الضوئي. من خلال الطرق المختبرية المتعددة للتشخيص، تبين أن 24 حالة يعانون فعلاً من التهاب السحايا. بينت النتائج أن 19 حالة (79%) يعانون من التهاب السحايا البكتيري وينقسمون إلى 11 حالة (46%) كانت نتيجة الزرع البكتيري موجبة وأن 8 حالات (33%) كانت نتيجة الزرع البكتيري سالبة بينما عد العدد المتبقي 5 حالات (21%) هو التهاب سحايا غير بكتيري. استنتجت الدراسة أن بالإمكان الاستفادة من قياس تركيز إنزيم اللاكتيت ديهيدروجينيز في السائل المخي الشوكي للتفريق بين نوعي التهاب السحايا إذ أنه يرتفع معنوياً في حالة التهاب السحايا البكتيري.