

## Some Biochemical and Cellular laboratory Indicators in the Cerebral Spinal Fluid among Suspected Bacterial Meningitis Patients

بعض المؤشرات المختبرية البايوكيميائية والخلوية في السائل الشوكي الدماغى بين مرضى التهاب السحايا الجرثومى المشتبه بهم.

Enám Ab. Al-Jabber Rasol\*

Prof. Dr. Baqur A.Sultan \*\*

Prof. Dr. Hayder k. Hassoun\*\*\*

الخلاصة:

**خلفية البحث:** أجريت هذه الدراسة على ٢٠٠ طفل وبالغ من كلا الجنسين الذين راجعوا مستشفى الزهراء التعليمي للولادة والاطفال ومركز الفرات الأوسط للأمراض العصبية في محافظة النجف من تموز ٢٠١٦ إلى تموز ٢٠١٧ لمعاناتهم من بعض الأعراض التي قد تكون ذات صلة بالتهاب السحايا، كان متوسط أعمار المرضى المشتبه بهم ١٣.٠٩ سنة للذكور (١٠٩)، و ١١.٢٨ سنة للإناث (٩١).

**الهدف:** تحديد الاختبارات الكيميائية الحيوية ( مستوى الكوكوز و البروتين ) ، وكذلك عد خلايا الدم البيضاء ( الخلايا للمفاوية والعدلات ) في مرضى التهاب السحايا .

**المنهجية:** تم إجراء الفحص الكيميائي الحيوي لسائل النخاع الشوكي (مستوى الكوكوز والبروتين) ، وكذلك عدد خلايا الدم البيضاء (الخلايا للمفاوية والعدلات)، وأجريت هذه الدراسة للفترة من حزيران ٢٠١٦ إلى حزيران ٢٠١٧ . وقد أجريت جميع الفحوصات البايوكيميائية (الكوكوز و البروتين ) و عد الخلايا لسائل النخاع الشوكي و عمل المسحات المباشرة وصبغها بصبغة كرام و اضافة الى ذلك تم زرع العينات بمزارع خاصة لجميع المشمولين بالدراسة . وكان متوسط مستوى الجلوكوز في السائل النخاعي من مرضى التهاب السحايا ٦٢.٥٤ ملغ / دل. في حين كان متوسط مستوى البروتين الكلي في السائل النخاعي من مرضى التهاب السحايا ٢٧.٢٣ ملغ / دل. نسب الخلايا المتعادلة والمفاوية كانت هي السائدة في نفس السائل الشوكي للمرضى

**النتائج:** كان متوسط مستوى الجلوكوز في السائل النخاعي الشوكي لمرضى التهاب السحايا ٦٢.٥٤ ملغ / ديسيلتر. و كان متوسط مستوى البروتين الكلي ٢٧.٢٣ ملجم / ديسيلتر ، كانت العدلات هي الخلية السائدة لجميع مرضى التهاب السحايا المشتبه بهم.

**الاستنتاجات:** ١. يمكن استخدام الاختبارات الكيميائية الموجبة في تحليل سائل النخاع الشوكي للتمييز بين التهاب السحايا الجرثومي وغير الجرثومي. ٢. لا يعتمد التهاب السحايا الجرثومي الإيجابي على نتيجة السكر والبروتين في سائل النخاع الشوكي فقط. **التوصيات:** إعطاء الأولوية للمراجعة المبكرة للمريض وإجراء التحاليل المختبرية.

### ABSTRACT:

**Background:** This study was conducted on 200 children and adult of both sexes who attended Al- Zahra Maternity and Children Teaching Hospital & Middle Euphrates Neuroscience Center in Al-Najaf province from July 2016 to July 2017 because they complaining of some symptoms that may related to meninges infection. The mean ages of suspected patients were 13.09 years for males (109), and 11.28 years for females (91).

**Aim of study:** Identification of biochemical contents (glucose and protein level) and cell count (neutrophil and lymphocyte) of CSF among patients with meningitis.

**Methodology:** The biochemical examination of spinal cord fluid (glucose and protein level), as well as the number of white blood cells (lymphocytes and rectangles), was conducted for the period from June 2016 to June 2017. All the biochemical tests (glucose and protein), counting the cells of the spinal cord fluid, making the direct swabs and dyeing them with chromium were done. In addition, the samples were planted with special farms for all the subjects. The average glucose level in cerebrospinal fluid of meningitis patients was 62.54 mg / dl. While the mean total protein level in CSF of meningitis patients was 27.23 mg / dl. Equivalent and lymphatic cell counts were predominant in the same spinal fluid of patients.

**Results:** The mean level of glucose in CSF of meningitis patients was 62.54 mg/dl. The mean level of total protein in CSF of meningitis patients was 27.23mg/dl. Neutrophil & lymphocyte was the predominant cell in CSF of all suspected meningitis patients.

**Conclusion:** The positive parameters in the analysis of CSF may be used to differentiate between bacterial and non- bacterial meningitis. Positive bacterial meningitis does not depend on the result of CSF sugar & protein only.

**Recommendation:** Give priority to medical soon attending and laboratory analysis

**Keyword:** CSF, bacterial meningitis, streptococcus pneumonia, Neisseria meningitides, Haemophilus influenza.

\* MSc. Dep. of Microbiology, college of Medicine, Kufa University. E-mail: [inamkashkol@gmail.com](mailto:inamkashkol@gmail.com)

\*\* Prof. of microbiology, College of Medicine, Kufa University

\*\*\* Prof. of clinical Neurology, college of medicine, Kufa University

### INTRODUCTION

Meningitis is defined as an inflammation of the protective membranes (meninges) that surround the brain and spinal cord <sup>(1)</sup>, the severity of the meningitis related with microbial causes that may be bacteria, viruses, mycobacteria, parasites and fungi <sup>(2)</sup>. The incidence of

meningitis is usually high in developing countries, with poor-socioeconomic status <sup>(3)</sup>, streptococcus pneumonia, Neisseria meningitides, and Haemophilus influenza are mostly detected with documented cases of community-acquired bacterial meningitis <sup>(4,5)</sup>. In bacterial meningitis, cell number is actually changed, especially the polymorph nuclear cells, as well as hypoglycorrhachia and high CSF protein concentration <sup>(6)</sup>. CSF glucose normally decreases in about 75 % of meningitis cases <sup>(7)</sup>. An insignificant decrease in the CSF glucose concentration has been found in viral meningitis, tuberculosis meningitis associated with low CSF glucose level <sup>(8)</sup>. The CSF protein is typically increased in bacterial meningitis. The protein level higher than 500 mg/dl is strongly correlated with the expansion of neurological disorders <sup>(9)</sup>.

### AIM OF STUDY

Identification of biochemical contents (glucose and protein level) and cell count (neutrophil and lymphocyte) of CSF among patients with meningitis

### METHODOLOGY

The study was conducted on 200 patients of different ages and genders (109 males and 91 females) who attended as clinically suspected meningitis cases in AL-Najaf providence, from July 2016 to July 2017.

**CSF glucose test:** GLUC-PAP (Glucose Iquicolor) test was used for determination of glucose in CSF. It was done according to manufacturer instruction.

**CSF protein test:** (Total protein liquicolor) Photometric colorimetric test was used for total proteins of CSF, it was done according to manufacturer instruction`

**CSF W.B.Cs. count:** The cell count of CSF was performed by neubauer chamber of white blood cells (lymphocyte and neutrophil).

### RESULTS:

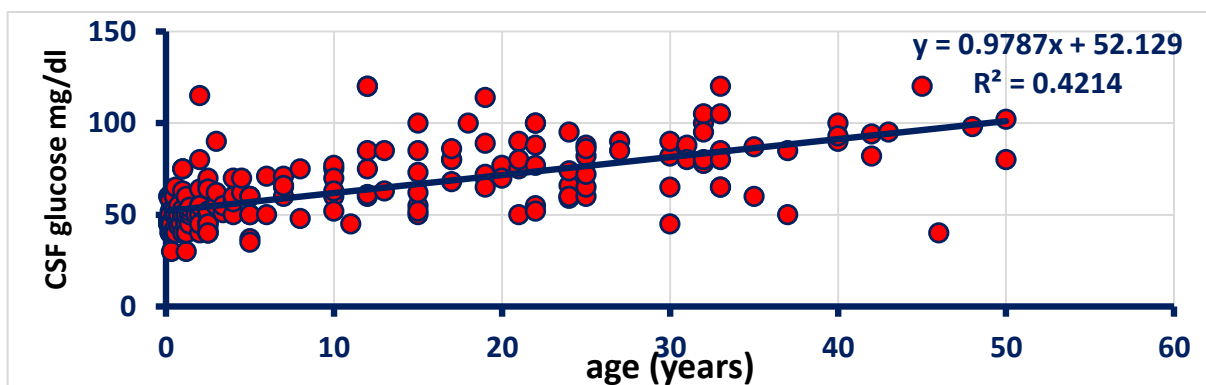
**1- CSF glucose level:** CSF glucose level of suspected meningitis patients according to age group.

**Table (1):** CSF glucose level of suspected meningitis patients according to age groups

CSF glucose						
	No.	Mean mg/dl	Std. Deviation mg/dl	Std. Error mg/dl	Minimum mg/dl	Maximum mg/dl
>1 Y	37	48.16	7.77	1.27	30.00	65.00
1-9 Y	73	54.42	13.65	1.59	30.00	115.00
10-19Y	32	75.37	19.49	3.44	45.00	120.00
20-29 Y	26	75.23	14.75	2.89	50.00	100.00
30-39 Y	21	81.42	18.57	4.05	45.00	120.00
40 Y ≤	11	90.36	19.80	5.97	40.00	120.00
Total	<b>200</b>	<b>64.13</b>	<b>20.18</b>	<b>1.42</b>	<b>30.00</b>	<b>120.00</b>

The mean of the glucose level was 48.16 - 90.36 in less than one year age groups, while the minimum and maximum value were 30.00 and 120.00 mg/dl respectively (table1, Figure1).

**Figures (1):** The correlation of age group with CSF glucose level



2- **CSF Protein level:** CSF protein level of suspected meningitis patients according to age groups.

**Table (2):** CSF protein level of suspected meningitis patients according to age groups

Descriptive						
CSF protein						
	No.	Mean mg/dl	Std. Deviation mg/dl	Std. Error mg/dl	Minimum mg/dl	Maximum mg/dl
>1 Y	37	24.94	9.74	1.60	10.00	45.00
1-9 Y	73	26.73	11.72	1.37	9.00	54.00
10-19Y	32	29.06	11.43	2.02	15.00	60.00
20-29 Y	26	31.50	12.55	2.46	15.00	60.00
30-39 Y	21	31.42	10.97	2.39	14.00	50.00
40 Y <	11	37.81	15.50	4.67	15.00	65.00
<b>Total</b>	<b>200</b>	<b>28.50</b>	<b>11.90</b>	<b>0.84</b>	<b>9.00</b>	<b>65.00</b>

The mean of the protein level was 28.94 - 37. 8 mg/dl in less than 1 year age groups, while the minimum and maximum values were 9.00 and 650.00 mg/dl respectively (table 2).

3- **CSF W.B.Cs. count.**

1- **CSF neutrophil count:** CSF neutrophil count of suspected meningitis patients according to age groups

**Table (3):** CSF neutrophils count in suspected meningitis patients of according to age groups.

Descriptive						
Neutrophil						
	No.	Mean cell/mm <sup>3</sup>	Std. Deviation cell/mm <sup>3</sup>	Std. Error cell/mm <sup>3</sup>	Minimum cell/mm <sup>3</sup>	Maximum cell/mm <sup>3</sup>
>1 Y	37	71.89	124.97	20.54	0.00	500.00
1-9 Y	73	52.20	67.76	7.93	0.00	280.00
10-19Y	32	64.62	104.48	18.47	0.00	500.00
20-29 Y	26	36.84	36.98	7.25	0.00	150.00
30-39 Y	21	32.90	34.98	7.63	0.00	100.00

40 Y <	11	58.18	43.08	12.99	10.00	150.00
Total	<b>200</b>	<b>54.14</b>	<b>82.10</b>	<b>5.80</b>	<b>0.00</b>	<b>500.00</b>

The mean value of neutrophil according to ages was 71.89-58.18 cell/mm<sup>3</sup>. It increased in age groups (less than 1 year) and the minimum & maximum values were 00.00 and 150.00 cell/mm<sup>3</sup> respectively.

**2- CSF lymphocyte count:** CSF lymphocyte count of suspected meningitis patients according to age groups

**Table (4):** CSF lymphocyte count in suspected meningitis patients of according to age groups

Descriptive						
Lymphocyte						
	No.	Mean cell/mm <sup>3</sup>	Std. Deviation cell/mm <sup>3</sup>	Std. Error cell/mm <sup>3</sup>	Minimum cell/mm <sup>3</sup>	Maximum cell/mm <sup>3</sup>
>1 Y	37	33.64	63.73	10.47	0.00	300.00
1-9 Y	73	28.19	44.37	5.19	0.00	200.00
10-19Y	32	23.37	29.52	5.21	0.00	100.00
20-29 Y	26	38.50	63.80	12.51	0.00	200.00
30-39 Y	21	43.61	68.00	14.84	0.00	200.00
40 Y <	11	46.36	60.01	18.09	2.00	200.00
Total	<b>200</b>	<b>32.39</b>	<b>52.81</b>	<b>3.73</b>	<b>0.00</b>	<b>300.00</b>

The mean value of lymphocyte count according to ages was 33.64 – 46.36 cell/mm<sup>3</sup>. It increased in age groups 40 years and the minimum and maximum values were 00.00 and 300.00 cell/mm<sup>3</sup> respectively.

**DISCUSSION**

The current study was conducted on 200 suspected meningitis patients , attended Middle Euphrates Neuroscience Center & Al- Zahra Maternity and Children Teaching Hospital in Al-Najaf .The cases were firstly diagnosed by neuroscience specialist as suspected meningitis and glucose , protein and cell count were done for them.

Regarding the number of suspected patients, 109 patients (54.5%) was of males and 91patintes (45.5%) of females of different ages. This percentage is nearly corresponding to other research <sup>(10, 11)</sup> but not corresponding to <sup>(12)</sup>. The variation between the numbers of male and female patients are poorly understood except hypothesis that assumed the increased of male susceptibility may belong to immune deficiency <sup>(13)</sup>.

CSF glucose level was significantly decreased < 40 mg/dl) in patients with bacterial meningitis, this come agree with <sup>(14)</sup> in Iraq and <sup>(15)</sup> in Egypt, but the current result is not agree with result of <sup>(16)</sup>.

The variation of glucose level in meningitis may be due to glycolysis by both white cells and pathogen, or may be due to impaired CSF glucose transport through the blood - brain barrier <sup>(17)</sup>.

The CSF protein level was elevated more than 50 mg/dl in both suspected bacterial meningitis patients, this result comes agree with<sup>(15)</sup>, but disagree with other research <sup>(18,19)</sup>, who found the CSF protein level was higher in positive meningitis patients only. Also the current result of elevation of CSF protein level in positive meningitis cases was confirmed by

many searches <sup>(20)</sup> in Iraq, <sup>(21)</sup> in Egypt, <sup>(22)</sup> in Portugal, <sup>(23)</sup> in South Korea and <sup>(24)</sup> in Nepal, who referred to marked elevation of CSF protein level in bacterial meningitis patients only.

It was found significant ( $p=0.007$ ) predominant of neutrophils in CSF of positive bacterial meningitis patients when compared with lymphocytes, and this predominant count of neutrophils was insignificant ( $p= >0.05$ ) among different positive bacterial meningitis (N. meningitis, S. pneumoniae, and H. influenza). This result was in agreement with the results of author <sup>(21)</sup>, but not in agreement with other author <sup>(25)</sup>. The increase of neutrophils in CSF of positive cases occurs due to infection although several authors have demonstrated, that the CSF neutrophils cannot be distinguished between bacterial and non-bacterial meningitis <sup>(26)</sup>.

## CONCLUSION

The positive parameters in the analysis of CSF may be used to differentiate between bacterial and non- bacterial meningitis, Positive bacterial meningitis dose not dependable on the result of CSF sugar & protein only.

## RECOMMENDATION

Give priority to medical soon attending and laboratory analysis.

## REFERENCES:

1. Bloch, K. C. & Tang, Y.-W. , Molecular Approaches to the Diagnosis of Meningitis and Encephalitis. In: Persing, D. H. (Ed.) *Molecular Microbiology: Diagnostic Principles and Practice*. (2011). 2nd Ed. Washington D.C.: ASM Press
2. CDC. Bacterial Meningitis [Online]. Available: <http://www.cdc.gov/meningitis/bacterial>. (2012). Html [Accessed 15-01-2014 2014].
3. M. C. Brouwer, A. R. Tunkel, and D. Van De Beek, "Epidemiology, Diagnosis, and Antimicrobial Treatment of Acute Bacterial Meningitis," *Clinical Microbiology Reviews*, (2010) Vol. 23, No. 3, Pp. 467–492.
4. S. A. Namani, R. A. Koci, E. Qehaja-Buc, Aj, L. Ajazaj-Berisha, And M. Mehmeti, "The Epidemiology Of Bacterial Meningitis In Kosovo," *Journal Of Infection In Developing Countries*, (2014) Vol. 8, No. 7, Pp. 823–830,.
5. G. M. K. Abdeldaim, K. Str°alin, J. Korsgaard, J. Blomberg, C. Welinder-Olsson, And B. Herrmann, "Multiplex Quantitative Pcr For Detection Of Lower Respiratory Tract Infection And Meningitis Caused By Streptococcus Pneumoniae, Haemophilus Influenzae And Neisseria Meningitidis," *Bmc Microbiology*, (2010) Vol. 10, Article 310,.
6. Venkatesan, A. & Griffin, D. E. Chapter 20 - Bacterial Infections. In: Irani, D. N. (Ed.) *Cerebrospinal Fluid in Clinical Practice*. (2009). Philadelphia: W.B. Saunders.
7. Dubos F, Korczowski B, Aygun Da, Martinot A, Prat C, Galetto-Lacour A, Casado-Flores J, Taskin E, Leclerc F, Rodrigo C, Gervaix A, Leroy S, Gendrel D, Bréart G, Chalumeau M.:Serum Procalcitonin Level And Other Biological Markers To Distinguish Between Bacterial And Aseptic Meningitis In Children: A European Multicenter Case Cohort Study. *Arch Pediatr Adolesc Med*. (2008) Dec; 162(12):1157-63. Doi: 10.1001 /Archped i.162.1 2. 1157.
8. Fischbach, Ravel, *Laboratory Medicine*. (2009). In: 3 (Ed.). London: Wiley.
9. Nigrovic, MD MPH, Lise E.; Kimia MD, Amir A.; Shah MD MSCE, Samir S.; Neuman MD MPH, Mark I "Relationship between Cerebrospinal Fluid Glucose and Serum Glucose". *The New England Journal of Medicine*. (2012). 366: 576-578. doi:10.1056/NEJMc1111080
10. Muhi Kadhem Al-Janabi, Jassem Muhammed Salih Al – Mawali, Shatha Ahmed Muhammed Ali: Iraqi Children with Acute Bacterial Meningitis. Who May Need Ventilatory Support, Children With Acute Bacterial M, (2008) VOL.7, NO. 2,

11. Kala Yadhav ML. Study of Bacterial Meningitis in Children Below 5 Years with Comparative Evaluation of Gram Staining, Culture and Bacterial Antigen Detection. *J Clin Diagn Res.* (2014) 8(4):04–06.
12. Mosavi-Jarrahi A., Esteghamati A., Asgari F., Heidarnia M., Mousavi-Jarrahi Y, Goya M. Temporal Analysis of the Incidence of Meningitis in the Tehran Metropolitan Area, 1999-2005. *Popul Health Metr.* (2009)7:19.
13. Fish EN. The X-files in immunity: sex-based differences predispose immune responses. *Nat Rev Immunol* (2008); 8:737e44.
14. Haider Nadhim Abd:Acute Meningitis in Children: Clinical and Laboratory Profiles college of medicine al-Mustansiriyah university. ( 2013) QMJ VOL.9 No.16
15. Walaa Shawky, Khater and Safia Hamed Elabd:Identification of Common Bacterial Pathogens Causing Meningitis in Culture-Negative Cerebrospinal Fluid Samples Using Real-Time Polymerase Chain Reaction Volume, Article ID ( 2016)4197187, 5 pages <http://dx.doi.org/10.1155/2016/4197187>
16. Sormunen P, Kallio MJ, Kilpi T. C-reactive protein is useful in distinguishing Gram stain-negative bacterial meningitis from viral meningitis in children. *J Pediatr.* 1999, 134: 725-729.
17. Nigrovic, MD MPH, Lise E.; Kimia MD, Amir A.; Shah MD MSCE, Samir S.; Neuman MD MPH, Mark I.:"Relationship Between Cerebrospinal Fluid Glucose And Serum Glucose". *The New England Journal of Medicine.* (2010), 366: 576-578. Doi: 10.1056/Nejm1111080. NII, N. N. F. I. I. *Pneumococcal* [Online]. Available:
18. Mehmet Ceyhan, Inci Yildirim, Paul Balmer, Ray Borrow, Bunyamin Dikici, Mehmet Turgut, Nese Kurt, Aysel Aydogan, Cigdem Ecevit, Yasar Anlar, Ozlem Gulumser, Gonul Tanir, Nuran Salman, Nezahat Gurler, Nevin Hatipoglu, Mustafa Hacimustafaoglu, Solmaz Celebi, Yavuz Coskun, Emre Alhan, Umit Celik, Yildiz Camcioglu, Gulden Secmeer, Deniz Gur, and Steve Gray: A Prospective Study of Etiology of Childhood Acute Bacterial Meningitis, Turkey ; *Emerging Infectious Diseases* (2008) • [www.cdc.gov/eid](http://www.cdc.gov/eid) • Vol. 14, No. 7, DOI: 10.3201/eid1407.070938
19. Russul Feihan Mussa: The Significance of Serum C-Reactive Protein in Childhood Acute Meningitis College of Medicine, University of Babylon, Hilla, IRAQ *Medical 3 Journal of Babylon*, (2015) Vol. 12- No. 3: 730-738, <http://www.medicaljb.com> ISSN 2312-6760 ©2015 University of Babylon
20. Seenaa Muhammed Ali 1, Heersh Hma Raof Saeed 2, Khalid Rashid Suliman (2017): *Meningitis in Sulaimani Pediatric Teaching Hospital: A Retrospective Study Mustansiriya Medical Journal* Volume 16 Issue 2.
21. Rabab F., Marwa K., Waleed F. (2014). Role of Clinical Presentations and Routine CSF Analysis in the Rapid Diagnosis of Acute Bacterial Meningitis in Cases of Negative Gram Stained Smears. *Journal of Tropical Medicine.* Article ID 213762.
22. Sofia Á., Teresa C., Ana M. *Prediction Of Bacterial Meningitis Based On Cerebrospinal Fluid Pleocytosis In Children. The Brazilian Journal Of Inf.* (2013) *Digno.* 17 (4):401–404.
23. Jungpyo L., Hyeon K., Joon S. L., Heung D. K., Hoon-Chul K.. Applying The Bacterial Meningitis Score in Children with Cerebrospinal Fluid Pleocytosis: A Single Center's Experience. *Korean J Pediatr.* (2015): 58(7):251255.
24. Kalpana K. M., Tejesh M., Seshagiri R., Sahisnuta B., Ravi S. Is Cerebrospinal Fluid C - reactive protein a Better Tool than Blood C - reactive protein in Laboratory Diagnosis of Meningitis in Children? *Sultan Qaboos University Med. J* (2013). 13, Iss. 1: 93-99.
25. Majeed Arsheed Sabbah1, Ghusoon A. Abdulhasan2, Kifah A. Jasem3, and Hayfa H. Hassani: Quantification of H. influenzae Type b in cerebrospinal fluid from children with meningitis *Int.J.Curr.Microbiol.* (2014) *App.Sci* 3(3): 283-290 2319-7706 Volume 3 Number 3 (2014) pp. 283-290
26. Chenghong Lei, Thereza AS, Yongsoon S, et al.: Enzyme specific activity in functionalized nanoporous supports. *Nanotechnology*; (2008), 19:125102.