

Correlation between Interleukin(IL-6) and Procalcitonin (PCT) Level among Diarrheal Children

Nihad Khalawe Tektook¹, Ahmed Salim Hadi Al-Khafaji²

¹Assist Prof Middle Technical University / College of Medical & Health Technology, Medical Laboratory Techniques Dep., ² Pediatrics Specialist, Iraqi Board In Pediatrics, Karbala Pediatric Teaching Hospital/Karbala Health Directorate/Iraq

Abstract

This study was conducted his study was conducted in Baghdad for the period from December 1, 2019 to June 3, 2020 for determination of the level of elevation of interleukin-6 and procalcitonin in children with acute diarrhea, I was included 50 children suffering from diarrhea and 50 children without any other disease, where the ages of children in both groups ranged from one month to five years. The study included collecting information from children in both groups, including gender, age, living situation, number of family members, standard of living and social as well as the number of family members, number of rooms in the house. Amount of 5 ml of blood samples were collected from all the children included in this study, where the blood samples were separated by the centrifuge device and the serum samples were separated from them and kept in the refrigerator until the tests for detecting the level of Interleukin 6 and procalcitonin using ELISA technique. In this study, 76 % of diarrheal children were suffered from abdominal pain, 68% with dehydration, 58% of fever, 46% had vomiting. The presented study found that, 78% of families with diarrheal children were lived in crowded houses, 73% didn't wash vegetables before eat, 69% haven't wash hands, 66 used tap water for drinking. In this study, IL-6 was observed in elevated mean in diarrheal children (19.66 ± 2.19 ng/ml), when it compared with the control healthy children (4.27 ± 1.46 ng/ml) ($P < 0.001$). In this study, procalcitonin was also observed in elevated mean in diarrheal children (42.17 ± 9.28 ng/ml), when it compared with the control healthy children (28.19 ± 8.27 ng/ml) ($P < 0.001$). The study showed that the maximum means of PCT and IL-6 in diarrheal children were observed in those with fever, followed by abdominal pain. The study revealed a significant positive correlation between IL-6 and PCT level among diarrheal children. **Conclusions:** The study showed a significant relation of PCT and IL-6 with diarrhea..

Keywords: Procalcitonin; diarrhea; IL-6; Abdominal pain

Introduction

Diarrhea is one of the most common diseases among children in various parts of the world, although it is considered one of the common diseases that its severity is almost limited, and this risk is that children are afflicted with what is called the term dehydration, which leads to the loss of salts and water from the body through the digestive system and abroad The risk of developing dehydration in children increases in children under five years of age ⁽¹⁾.

Diarrhea is of two types, and they are acute diarrhea, the period of which increases to more than 14 days from the date of injury and chronic diarrhea, and it is not when the patient suffers from diarrhea for a period longer than that⁽²⁾. It is also classified according to the persistence of stool in children into two types of watery diarrhea, which results from injuries in microorganisms Like bacteria, viruses, and parasites, the infection is often in the upper part of the intestine, and the stool is liquid, which may cause dehydration.

Bacteria such as *Escherichia coli*, *salmonella*, *shigella*, and *V.cholera*, predominately cause acute diarrhea, in addition to viral infection also could be on of causes of watery diarrhea plus vomiting and

Corresponding author:

Nihad Khalawe Tektook

Gmail:drnihadkhalawe@gmail.com

fever in children with gastroenteritis^(3,4). Interleukin-6 is considered one of the most important inflammatory factors among the types of cytokines in the body, which are raised due to infection with bacteria, viruses or parasites in the body.⁽³⁾. Where the scientific evidence indicates that the high level of interleukin 6 in children with diarrhea may be caused by an acute bacterial or viral infection.

The level of interleukin 6 rises directly with the severity of infection in these children ⁽⁵⁾. In addition, the protein factor procalcitonin was found in recent studies to be high in bacterial infections, especially due to gram negative bacteria in diarrhea, urinary tract infection and bacteremia in people with this condition, as its height is directly proportional to the severity of the disease and is also directly proportional to the high level of interleukin. ^{6(6,7)}. This study was conducted for the purpose of determining the level of elevation of interleukin-6 and procalcitonin in children with acute diarrhea who are less than five years old and related to ages, their level of hygiene.

Patients and Methods

This study was conducted in Baghdad for the period from December 1, 2019 to June 3, 2020, and included 50 children suffering from diarrhea and 50 children without any other disease, where the ages of children in both groups ranged from one month to five years. The study included collecting information from children in both groups, including gender, age, living situation, number of family members, standard of living and social as well as the number of family members, number of rooms in the house. Amount of 5 ml of blood samples were collected from all the children included in this study, where the blood samples were separated by the centrifuge device and the serum samples were separated from them and kept in the refrigerator until the tests for detecting the level of Interleukin 6 and procalcitonin using ELISA technique.

Results

In this study, 44% of studied children were within the age group <1 year followed by 36% in the age group 1-2 year, 27 of 50 were females and 55% rurals, (Table 1).

Table 1: general characteristics of studied children

Age groups (year)	No.(%)
<1	22 (44%)
1-2	18 (36%)
3-5	10 (20%)
Total	50 (100%)
Sex	Male 23, female 27
Residence	55% rural

In this study, 76 % of diarrheal children were suffered from abdominal pain, 68% with dehydration, 58% of fever, 46% had vomiting, Figure 1.

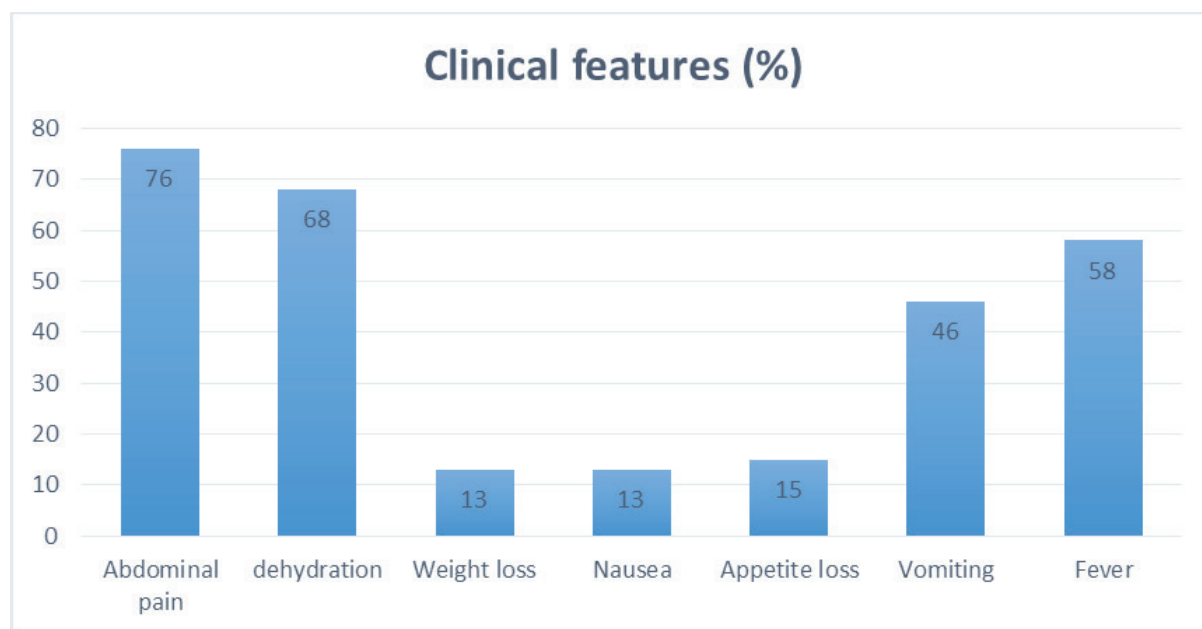


Figure 1: Clinical features of diarrheal children

The presented study found that, 78% of families with diarrheal children were lived in crowded houses, 73% didn't wash vegetables before eat, 69% haven't wash hands, 66 used tap water for drinking (Figure 2).

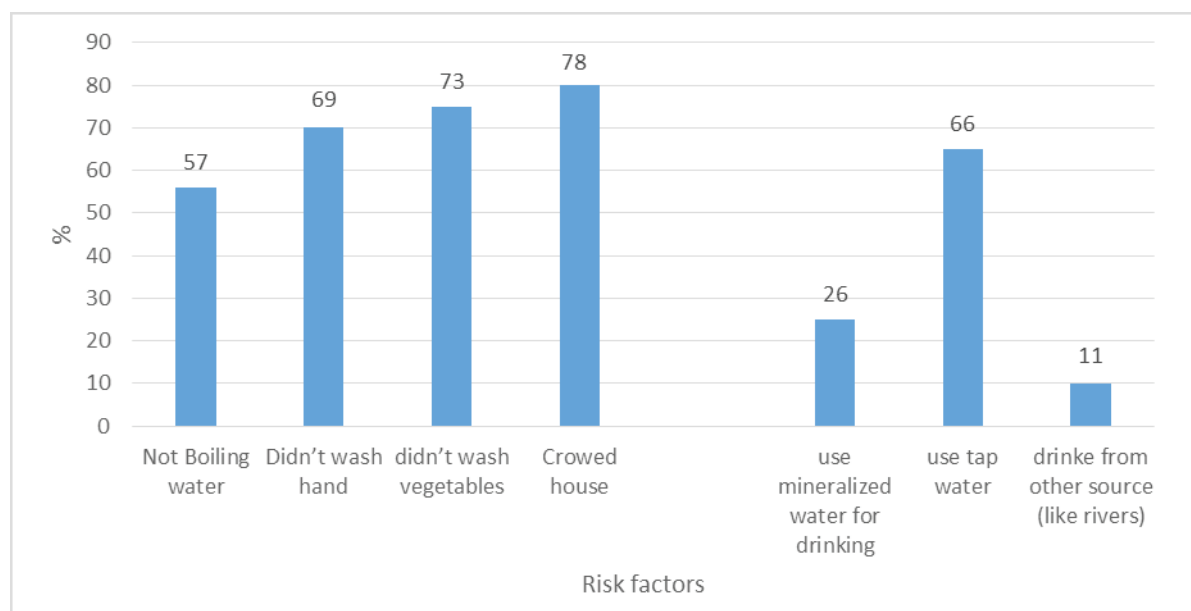


Figure 2: Risk factors of diarrheal children

In this study, IL-16 was observed in elevated mean in diarrheal children (19.66 ± 2.19 ng/ml), when it compared with the control healthy children (4.27 ± 1.46 ng/ml) ($P < 0.001$), Table 2.

Table 2: Level of IL-6 in children groups with and without diarrhea

Studied children	Interleukin-6 (ng/ml)	
	Mean	SD
With diarrhea (n:50)	19.66	2.19
Healthy children, (n:50)	4.27	1.46

P<0.001

In this study, procalcitonin was also observed in elevated mean in diarrheal children (42.17 ± 9.28 ng/ml), when it compared with the control healthy children (28.19 ± 8.27 ng/ml) (P<0.001), Table 3.

Table 3: Level of PCT in children groups with and without diarrhea

Studied children	Procalcitonin (ng/ml)	
	Mean	SD
With diarrhea (n:50)	42.17	9.28
Healthy children, (n:50)	28.19	8.27

P<0.001

The study showed that the maximum means of PCT and IL-6 in diarrheal children were observed in those with fever, followed by abdominal pain, Table 4

Table 4: relation of IL-6 and PCT with symptoms of diarrhea

Parameter	dehydration	Vomiting	Fever	Abdominal pain	P. value
PCT	33.4	30.5	46.7	38.5	0.001
IL-6	17.56	18.5	28.4	25.4	0.001

The study revealed a significant positive correlation between IL-6 and PCT level among diarrheal children, Figure 3.

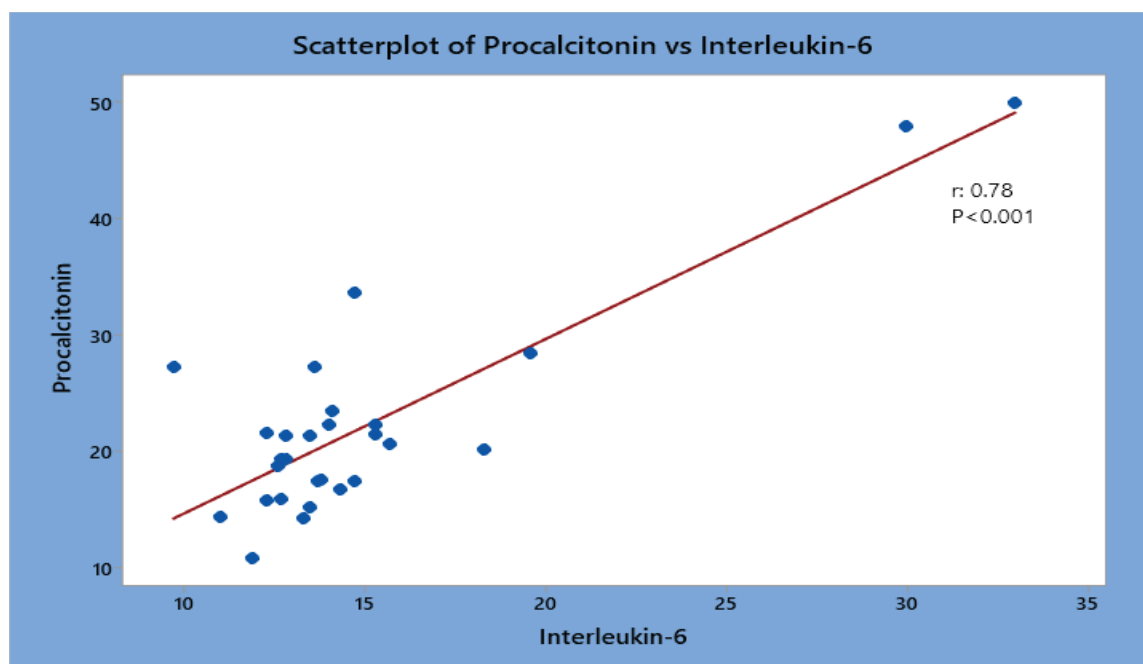


Figure 3: correlation between IL-6 and PCT level among diarrheal children

Discussion

In this study, 44% of studied children were within the age group <1 year followed by 36% in the age group 1-2 year, 27 of 50 were females and 55% rurals,(Table 1).In line with this study that there are many studies that have proven that diarrhea in children often occurs at young ages of less than five years, especially in those who are less than two years of age. A study conducted in previous decades or previous years stated that children who are less than two years old are More vulnerable to acute diarrhea due to bacteria or viruses (⁶⁻⁸).In this study, 76 % of diarrheal children were suffered from abdominal pain, 68% with dehydration, 58% of fever, 46% had vomiting, Figure 1.Dehydration and colic are among the most important symptoms of all ages, especially children, as past studies have shown that most children, and most of those children who are less than five years old and who suffer from severe diarrhea, were implicitly suffering from colic and dehydration, as well as high temperatures, which often accompany anorexia and thinness(^{9,10}).The presented study found that, 78% of families with diarrheal children were lived in crowded houses, 73% didn't wash vegetables before eat, 69% haven't wah hands, 66 used tap water for drinking (Figure 2).Past studies show that people or children

suffering from diarrhea, the majority of whom are families suffering from limited income and suffer from a disruption of the health system, and a high percentage of children with diarrhea do not wash their hands before eating and use running water for drinking (¹¹⁻¹⁴).In this study, IL-16 was observed in elevated mean in diarrheal children (19.66 ± 2.19 ng/ml), when it compared with the control healthy children (4.27 ± 1.46 ng/ml) ($P < 0.001$), Table 2.In line with this study, the study previously conducted in different countries of the world has shown that Interleukin-6 significantly increases blood serum in people with many diseases, including urinary tract infection, diarrhea, blood market store, and fever of unknown cause(¹⁵).In this study, procalcitonin was also observed in elevated mean in diarrheal children (42.17 ± 9.28 ng/ml), when it compared with the control healthy children (28.19 ± 8.27 ng/ml) ($P < 0.001$), Table 3.The study showed that the maximum means of PCT and IL-6 in diarrheal children were observed in those with fever, followed by abdominal pain, Table 4The study revealed a significant positive correlation between IL-6 and PCT level among diarrheal children, Figure 3.Where the level of interleukin-6 and the level of procalcitonin rises in people with acute diarrhea due to causes that lead to diarrhea such as the bacteria that cause diarrhea (¹⁶).Where the researcher(¹⁶)mentioned in his study that

the increase in the level of interleukin-6 came with an increase in the level of calcitonin, and the increase was proportional, meaning the higher the first, the higher the level of the second variable was very high, especially in children with diarrhea and those suffering from high temperatures⁽¹⁷⁾. The high temperatures in children with diarrhea are often due to the fact that the bacteria that cause diarrhea are of the type gram-negative bacteria, which contain endotoxins that in turn lead to elevated levels of interleukin-6, and the CRP and procalcitonin, which are automatically preserved as a result of infection in infected patients or any diseases, bacteremia, cough and urinary inflammation^(18&19). **Conclusions:** There was a significant relation of PCT and IL-6 with diarrhea.

Conflict of Interest: None

Source of Findings: None

Ethical Clearance: None

References

- Herlina H, Manoppo JI, Umboh A. Bacterial enteric pathogens and serum interleukin-6 levels in children with acute diarrhea. *Paediatrica Indonesiana*. 2016 Jul 1;56(3):144-8.
- Qin F, Wu H, Li X, Han J. Correlation between changes in gut flora and serum inflammatory factors in children with noninfectious diarrhea. *Journal of International Medical Research*. 2020 Jan;48(1):0300060519896154.
- Oyofa BA, Subekti D, Tjaniadi P, Machpud N, Komalarini S, Setiawan B, et al. Enteropathogens associated with acute diarrhea in community and hospital patients in Jakarta, Indonesia. *FEMS Immunol Med Microbiol*. 2002;34:139-46.
- Farthing M, Lindberg G, Dite P, Khalif I, Lindo ES, Ramakrishna BS, et al. *World Gastroenterology Organisation Practice Guidelines: acute diarrhea*. Milwaukee: World Gastroenterology Organisation; 2008. p. 1-29.
- Ahs JW, Tao W, Lofgren J, Forsberg BC. Diarrheal diseases in low- and middle-income countries: incidence, prevention and management. *Open Infect Dis J*. 2010;4:113-24.
- Yeung CY, Lee HC, Lin SP, Fang SB, Jiang CB, Huang FY, et al. Serum cytokines in differentiating between viral and bacterial enterocolitis. *Ann Trop Paediatr*. 2004;24:337-43.
- Das S, Anand D, Ray S, Bhargava S, Manocha A, Kankra M, Srivastava LM. Diagnostic accuracy of procalcitonin in proven and clinically suspected systemic infection. *Critical Care*. 2012 Jun;16(3):1-58.
- Hodges K, Gill R. Infectious diarrhea: cellular and molecular mechanisms. *Gut Microbes*. 2010;1:4-21.
- Hessle CC, Andersson B, Worl AE. Gram-positive and gram-negative bacteria elicit different patterns of pro-inflammatory cytokines in human monocytes. *Cytokine*. 2005;30:311-8.
- Lin CH, Hsieh CC, Chen SJ, Wu TC, Chung RL, Tang RB. The diagnostic value of serum interleukins 6 and 8 in children with acute gastroenteritis. *J Pediatr Gastroenterol Nutr*. 2006;43:25-9.
- Boga JA, Melon S, Nicieza I, Diego I, Villar M, Parra F, et al. Etiology of sporadic cases of pediatric acute gastroenteritis in Asturias, Spain, and genotyping and characterization of norovirus strains involved. *J Clin Microbiol*. 2004;42:2668-74.
- Johargy A, Ghazi H, Mumenah A. Frequency of viral, bacterial and parasitic enteropathogens among young children with acute diarrhoea in Saudi Arabia. *J Park Med Assoc*. 2010;60:456.
- Hsu TR, Chen SJ, Wu TC, Chung RL, Tang RB. Tumor necrosis factor- α and interleukin-10 in viral and bacterial gastroenteritis in children. *J Chin Med Assoc*. 2005;68:250-3.
- Zherebtsova N, Valishin DA, Mavziutov AR. Proinflammatory cytokines in children with acute enteric infections caused by enterobacteria. *Zh Mikrobiol Epidemiol Immunobiol*. 2007;3:48-52.
- Stoycheva MS, Murdjeva MA. Correlation between serum levels of interleukin-1 β , interleukin-1RA, interleukin-6, interleukin-10, interleukin-12, tumor necrosis factor- α , and interferon- γ with

- some clinical and laboratory parameters in patients with salmonellosis. *Biotechnol Biotechnol Eq.* 2005;19:143-6.
16. Bian F, Wu YE, Zhang CL. Variation in the levels of IL-6 in pediatric patients with severe bacterial infectious diseases and correlation analysis between the levels of IL-6 and procalcitonin. *Experimental and Therapeutic Medicine.* 2017 Jun 1;13(6):3484-8.
 17. Nainggolan SC, Aman AK, Hanafie A. The Relationship Between The Level Of Interleukin-6 And Procalcitonin In Severe Sepsis Patients At The Adam Malik Hospital. *Indonesian Journal of Clinical Pathology And Medical Laboratory.* 2019 Apr 10;25(1):38-41.
 18. Stambas J, Lu C, Tripp RA. Innate and adaptive immune responses in respiratory virus infection: implications for the clinic. *Expert Review of Respiratory Medicine.* 2020 Nov 1;14(11):1141-7.
 19. Al-Asy HM, Gamal RM, Abd Albaset AM, Elsanosy MG, Mabrouk MM. New diagnostic biomarker in acute diarrhea due to bacterial infection in children. *International Journal of Pediatrics and Adolescent Medicine.* 2017 Jun 1;4(2):75-80.