Diagnostic Value of Chemical and Hematological Markers in Children Acute Abdominal Pain

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Acute appendicitis, acute appendicitis with peritoneal abscess, acute gastroenteritis, lymphadenitis and gastroduodenitis raises serious health problems in children. The purpose of this study consisted in screening of hematological and biochemical markers to establish their significance especially in the case of abdominal diseases with nonspecific or severe symptoms. Data were collected prospectively from 10750 hospitalized children, of which 2538 with abdominal pain, boys 39%, girls 61%, coming from different social backgrounds: 57.8% urban, and 42.2% rural areas. Children with symptoms of acute appendicitis (52.7%) prevailed. Hematological and biochemical parameters of blood were determined by spectrophotometric, potentiometric, immunological and electrical impedance methods. Results. The majority of children with acute abdominal pain investigate (2358) had white blood cells, sedimentation rate of erythrocytes, neutrophils and lymphocytes percentages and C-reactive protein level exceeded the maximum limit of reference. C-reactive protein values were higher in children with clinical suspicion of acute appendicitis and mesenteric lymphadenitis, this marker is the first that react in cases of inflammations and infections. Inflammatory markers analyzed separately taking have no diagnostic value. The levels of white blood cells, sedimentation rate of erythrocytes and C-reactive protein increased together with neutrophil/lymphocyte high ratio, helpful pediatrician to establish an accurate diagnosis in a shorter time for the correct management of acute abdominal diseases.

Keywords: acute abdominal disease, C-reactive protein, blood cells, natremia, potassemia

The pain is defined by the I.A.S.P. (International Association for the Study of Pain) as *an unpleasant emotional and sensory experience, given by a real or potential tissue lesion or a description with terms that refer to such a lesion* [1]. Anatomo-functional systems of the pain develop in the child still in intrauterine period and shall be definitive until the 30th week of pregnancy. Abdominal pain is a common problem in children involving a checkup from your family doctor or pediatrician. Acute abdominal pain is a challenge for physicians to establish a diagnosis in a timely fashion, so that treatment can be initiated quickly and prevented morbidity. Acute abdominal pain is usually severe, persistent with sudden onset, benign self-limiting, such as gastroenteritis, constipation or viral diseases [2] or that can lead to a medical or surgical emergency [3]. In most cases, abdominal pain can be diagnosed by history and physical examination. The pain may be frequently associated with nausea and vomiting, diarrhea, abdominal distention, fever and signs of shock (high heart rate, low blood pressure, sweating, and confusion). Age is a key factor in the assessment of the case, the incidence and symptoms of abdominal pain varies greatly with the spectrum of pediatric age and causes symptoms. High incidence of abdominal pain in children, wide range of anatomo-functional structures involved in its generation, requires that the necessary development of laboratory tests to assist the pediatrician to establish a correct diagnosis and the severity of the disease. Most studies recommend as inflammatory markers white blood cells (WBC), neutrophil (granulocytes, GR), lymphocyte (L), sedimentation rate of erythrocyte (ESR), neutrophil/lymphocyte ratio, and C - reactive protein (CRP) level [4-10].

The aim of this study was to perform the screening of biochemical and hematological markers in children hospitalized with acute abdominal pain and comparing the levels of these markers for different acute abdominal conditions.

Experimental part

The study group was represented by 10750 pediatric patients hospitalized in the *Sfântul Ioan* Clinical Emergency Hospital for Children in Galati within a period of 2 years, for various diseases, aged between 1-18 years. All patients were included in the study after they, or their legal representatives have signed an informed consent. Subjects who have not signed the informed consent form were excluded from study. For all patients were completed worksheets with respect to demographics, physiologic and pathologic data. For all patients of the study group has been carried out complete clinical examination, have been collected samples to peripheral blood for different laboratory determinations, biochemical (C-reactive protein, alkaline reserve, natremia, potassemia) and hematological (ESR, number of leukocytes, lymphocytes and neutrophils percentages). Biochemical determinations were performed using automatic biochemistry analyzer VITROS 950 and the reagents supplied by Ortho Clinical Diagnostics, Johnson-Johnson Company, UK. The analyzer uses dry technology on slides (analytical elements assembled in support of multi-layer polyester) for performing in vitro quantitative measurements of components in biological fluids (blood, urine). Dry technology allows performing the reactions successively, ensuring precision and accuracy of measurements reflectance spectrophotometric and colorimetric

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comparable with atomic adsorption spectrometry. Determination of concentration of sodium and potassium ions were made through the potentiometric method: a drop of serum for investigation and a drop of reference liquid deposited on each half of the slide; migrate toward the center of the paper deck. Stable liquid junction formed connects between the reference electrodes to the electrode in the sample. Ion-selective electrode for potassium is made from a membrane that contains valinomycin, an ionophore for potassium. Having cavity approximately equal with the diameter of the potassium ion, the ionophore allows the formation of a complex between these ions and valinomycin which causes changes in potential of the electrode. Ion-selective electrode for sodium contains methyl monensin (ionophore for sodium). The difference in potential between reference electrode and electrode in sample is proportional to the concentration of ion in the blood analyzed, expressed in mmol/L. Reference range for Na^+ is: 137-145 mmol/L and for K^+: 3.5-5.2 mmol/L. Serum concentration of ECO_2 (alkaline reserve) was determined by spectrophotometric method using the kit ECO_2 slides. ECO_2 is the sum of the concentrations of bicarbonate and carbon dioxide dissolved in the serum. Reference range is: 22-30 mmol/L. CRP determination was performed using automatic biochemistry analyzer Rx IMOLA by imunoturbidimetric method in which human protein C antibodies produces agglutination of the latex particles coated with CRP. Agglutination of the particles is proportional to the concentration of CRP that is determined turbidimetrically. Reference range is: 0-0.5 mg/dL. Hemoleucogram was performed with automatic hematology analyzer K CELLTAK MEK produced by Nikon Kohden 6400 Firentze SRL, Italy. The analyzer determined cells count (white blood cells, platelets and red blood cells) by electrical impedance method. Leukocytes formula consists in differentiation circulating total leukocytes in the blood in the five types of white cells, expressed as percentage and in absolute number, each of them performing a specific function. Leucocytes formula performed was carried out automatically by the analyzer. ESR was determined by manual method Westergreen, the reference range for children is 4-12 mm/h.

The data was analyzed using EXCEL 2007 and SPSS version 20 for windows software package. To analyze the data we used statistical procedures included: Pearson's correlation, ANOVA, T-test. Qualitative variables are presented as percent and quantitative variables as mean ± SD. Between groups, the differences were considered significant when $p < 0.05$.

Results and discussions

2537 (23.6%) of the total investigated children (10750) accused abdominal pain. The characteristic symptoms of acute abdominal pain have been observed at 2358 patients (21.9%), while those of chronic abdominal pain at 179 patients (1.7%). The batch of patients with acute pain was formed in 1439 girls (61%; mean age 11.5 years) and 919 boys (39%; mean age 9.8 years); girls/boys ratio 1.57/1. Distribution by age group showed a higher percentage of children included in the group 10-14 years (938 cases, 39.8%), followed by groups 5-9 years (621 cases, 26.3%) and 15-18 (511 cases, 21.7%). Age group between 0-5 years was represented by 288 children (12.2%). Depending on the environment of residence, children with acute abdominal pain originated mainly from urban areas 57.8% (1364 cases), compared to those in rural areas 42.2% (1173 cases), with an urban/rural ratio 1.37/1. The distribution of cases depending on the cause of the pain showed a higher prevalence of children with acute appendicitis (AA) 44.8% (1056 cases). Significantly lower prevalence was observed for acute appendicitis with peritoneal abscess (AAPA) 7.9% (187), gastroenteritis (GE) 9.3% (218), gastroduodenitis (GD) 8.6% (203), mesenteric lymphadenitis (ML) 5.3% (125) and other diseases 24.1% (569). Cases of AA prevailed in children aged over 5 years (99.4%), as those of AAPA (98.4), ML (87.2%) and GD (81.2%), unlike the cases of GE that had a higher prevalence in children under 5 years old (69.7%).

In tables 1 and 2 are listed the values of blood parameters analyzed in the case of children hospitalized for acute abdominal pain with symptoms of acute appendicitis, acute appendicitis and peritoneal abscess, gastroenteritis, gastroduodenitis and acute mesenteric lymphadenitis.

Figure 1 shows graphically the distribution of values of the percentage of neutrophils and lymphocytes depending on the type of acute abdominal disease.

Analytical data indicate significant statistical differences between the groups of patients with AA and AAPA ($p < 0.05$, table 1) and insignificant between the GD and GE ($p > 0.05$) for parameters WBC, ESR and CRP.

In children with acute appendicitis, acute gastroenteritis and gastroduodenitis, age was significantly correlated with the WBC and ESR ($p < 0,05$). Additionally, in children with acute gastroenteritis age was significantly correlated with the CRP ($r = 0.856$; $p = 0.029$). The batch of children with

Parameters	Acute appendicitis (AA)					Acute appendicitis with peritoneal abscess (AAPA)					p-value**
	No* (%)	Mean	Min.	Max.	DS***	No* (%)	Mean	Min.	Max.	DS***	
Total Leukocytes (WBC), x $10^3/\mu L$	310 (29.4)	12.31	2.70	26.70	3.40	103 (82.8)	14.45	9.50	25.20	4.47	0.001
C-reactive protein (CRP), mg/dL	485 (46)	3.03	0.33	25.00	2.08	125 (100)	9.59	1.60	25.00	8.21	0.012
Erythrocyte sedimentation rate (ESR), mm/h	952 (90.2)	18.90	5.00	100.00	11.00	122 (98)	25.35	4.00	90.00	20.64	0.008

*Number of children (Percentage) with biochemical and hematological parameters altered in blood; ** p-value is significant if < 0.05, ***DS - standard deviation

Table 1
COMPARISON OF CLINICAL AND PARACLINICAL PARAMETERS IN ACUTE APPENDICITIS AND ACUTE APPENDICITIS WITH PERITONEAL ABSCESS

Diagnostic	Parameters	No.* (%)	Mean	Min.	Max.	Std. Dev.**
Gastroducodenitis (GD)	Total Leukocyte (WBC), x $10^3/\mu L$	185 (91.2)	14.74	3.6	31.8	5.70
	C-reactive protein (CRP), mg/dL	180 (88.7)	4.63	1.87	9.0	2.50
	Erythrocyte sedimentation rate (ESR), mm/h	183 (90.1)	19.42	11	54	7.79
Gastroenteritis (GE)	Total Leukocytes (WBC), x $10^3/\mu L$	200 (96)	11.46	7.90	35.6	5.04
	C-reactive protein (CRP), mg/dL	218 (100)	4.82	1.34	9.00	2.93
	Erythrocyte sedimentation rate (ESR), mm/h	216 (99.3)	20.77	11.0	82.00	10.32
	Alkaline reserve (RA) (mmol/L)	216 (99,3)	17.16	8.00	21.00	2.89
	Natremia (Na^+), mmol/L	121 (55.6)	142.62	128.00	166.00	8.42
	Potassemia (K^+), mmol/L	117 (53.7)	5.17	2.10	7.80	1.07
Mesenteric lymphadenitis (ML)	Total Leukocytes (WBC), x $10^3/\mu L$	103 (82.8)	12.05	3.60	25.90	5.61
	C-reactive protein (CRP), mg/dL	125 (100)	2.83	1.52	6.21	2.26
	Erythrocyte sedimentation rate (ESR), mm/h	122 (98.0)	17.84	10.00	48.00	7.56

*Number of children (Percentage) with biochemical and hematological parameters altered in blood; **DS - standard deviation

Table 2
DESCRIPTIVE STATISTICS FOR PARACLINICAL PARAMETERS IN GASTRODUODENITIS, GASTROENTERITIS AND MESENTERIC LYMPHADENITIS

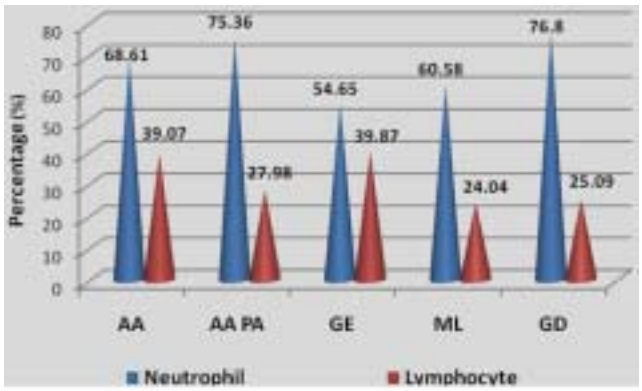

Fig. 1. Distribution of neutrophil and lymphocyte percentage values depending on the diagnosis

mesenteric lymphadenitis age was significantly correlated only with the WBC (r = -0.576; p = 0.001).

Acute appendicitis is characterized by inflammation of the cecal appendix and is the most common cause of acute abdomen both the child and the adult. Since there is no drug treatment of AA, diagnosis is necessary to be established quickly for the patient to be operated closer to the onset of disease. The evolution of AA, from the shape debut (catarrhal), to phlegmonous and gangrenous forms, the peritoneal wall is compromised and can occur perforation, postoperative recovery complicated and increases the risk of death. Positive diagnosis is mainly based on symptoms and physical examination. For patients with suspected appendicitis without classic manifestations [11] the doctor recommended laboratory tests that can support the diagnosis in advanced stages of AA and abdominal ultrasound. For children with abdominal pain and suspicion of AA, we performed laboratory tests of blood for the number of neutrophils, the total number of leukocytes, and reactive C protein and sedimentation rate of erythrocytes. The results of these tests indicate values that does not fit into the ranges of variation recommended for all analyzed parameters (GR, WBC, CRP and ESR; Table 1). Thus, the number of neutrophils has ranged from 25.6% to 97% in the case of acute appendicitis and from 30.3% to 92.1% in case of AAPA; most of the values were outside the range of normal (42-85%). It is known that neutrophils help the body in the fight against infection and the healing of the lesions; increase in neutrophils appears as a necessary reaction to the body, while it tries to heal or to remove an invading microorganism or a foreign substance. The increase of the number of neutrophils and their activity can be determined by bacterial, viral, fungal and parasitic infections, as well as inflammatory disorders, including autoimmune diseases and certain medications. For this reason it is believed that neutrophils alone cannot be considered a reliable parameter in the diagnostic for appendicitis in children [9]. However, some authors recommend neutrophil/lymphocyte ratio (GR/L) as a sensitive marker in the diagnosis of appendicitis in children, values of the ratio GR/ L higher than 3.5 and can be used in prediction of acute appendicitis [9, 12-14]. Values of GR/L greater than 8 are positive predictive values for gangrenous appendicitis [15, 16] having a higher sensitivity than leukocytosis. WBC count greater than the mean value ± standard deviation or a value greater than 9500 cells per μL in children is defined as Leukocytosis. In both forms of appendicitis total numbers of leukocytes observed by us

have overtaken 2.8 and 2.7 times the upper limit of the normal range (4000-9500 cells per μL) in the case of acute appendicitis and acute appendicitis with peritoneal abscess respectively. The total number of leukocytes has diagnostic value only in combination with high levels of CRP, with population of neutrophils and increased GR/L ratio [12, 17-22].

C-reactive protein is a protein synthesized by the liver whose blood levels are increased in inflammation. In the case of both forms of appendicitis C-reactive protein levels (CRP) exceeded the recommended maximum level (0.5 mg/dL). CRP test shows that levels of this protein were consistent with the severity of appendicitis, the average values are approximately 3 times higher in the case of AAPA, compared with acute appendicitis. Our results confirm those reported by Yokoyama [23] and Grönroos [6] which recommends increased levels of CRP as a marker of surgical indication for AA. C-reactive protein is not a diagnostic test but may help confirm the diagnosis in patients with atypical presentation. CRP is often used as an inflammatory marker not only in case of acute appendicitis [10, 23, 24, 25], but in other inflammatory diseases [26, 27]. Very high levels of CRP in patients with appendicitis indicate to form gangrenous disease progression, particularly if associated with leukocytosis and neutrophilia. WBC greater than 12,000/mm^3 together with CRP and greater than 3 mg/dL increase the likelihood of appendicitis [28, 29]. In most patients with suspected AA (90.2%) and AAPP (92.3%), ESR values found us (table 1), have exceeded the maximum permissible limit for children (4-12 mm/h). High levels of ESR are explained by increased plasmatic levels of acute phase proteins (α-globulins, fibrinogen) or immunoglobulins in inflammatory diseases and infections [30, 31].

Mesenteric lymphadenitis refers to inflammation of the mesenteric lymph nodes [32. 33] accompanying bacterial (*Y. pseudotuberculosis* and *Y. enterolitica*, *Helicobacter jejuni*, *Campylobacter jejuni*, *Salmonella* and *Shigella* spp.) and viral infections (adenovirus, rotavirus, cytomegalovirus). It causes clinical symptoms that often are difficult to differentiate from other abdominal diseases, especially acute appendicitis. The exact incidence of lymph node disorders is not known, because the data recorded usually refers to associated disease, not lymphadenopathy. Lymphadenopathy is estimated at 38-45% of children [34], mainly as a result of infection [35], making it one of the most common problems in clinical pediatrics [36]. Diagnostic tests are aimed at confirming the source of infection and inflammation. Within the framework of our study 125 children (5.3%) under the age of 18 years were suspected of lymphadenitis. ESR, CRP, WBC and GR markers which were investigated to determine the degree of inflammation, showed elevated values at 82.8-100% patients; CRP showing the highest sensitivity (table 2).

In our study, 218 (9.3%) of pediatric patients showed specific signs and symptoms of acute gastroenteritis, which remains a major cause of morbidity and mortality in children worldwide representing 15% of deaths of children [37]. GE is an infection of the intestines that causes diarrhea, nausea, vomiting, abdominal cramps, fever, and reduced appetite. Intestinal infections are caused of viruses [rotavirus: 75-90%] and bacteria (*Campylobacter* spp., *Salmonella* spp., *Escherichia coli*, *Shigella* spp., *Clostridium difficile, Vibrio cholerae*) and can lead to dehydration. Laboratory tests carried out by us has shown elevated values for all inflammatory markers at the majority of children with GE, which confirms the bacterial and viral nature of disease.

In the case of acute GE, the most sensitive acute phase reagents were: CRP (100% cases), ESR (99.3%) and WBC (96%), 59.6% of children with acute GE showed increased levels of neutrophil count and 53.7% in the number of lymphocytes (table 2). CRP levels found new results confirm the findings of other authors [38-40], indicating higher levels for this parameter in the case bacterial infection as compared with those viral. Determination of the concentration of serum C-reactive protein permits early differentiation between bacterial and viral GE, the positive predictive value for this parameter alone is ≥ 2 mg/dL [40]. In addition, the measurement of inflammatory markers we have investigated and levels of serum electrolytes (sodium and potassium), because the diarrhea and vomiting are symptoms in acute GE. GE in children tested caused both hyponatremia (sodium levels in the blood stream less than 137 mmol/L) and hypokalemia (potassium levels < 3.5 mmol/L) and hypernatremia (sodium levels in the blood stream > 145 mmol/L) and hyperkalemia (potassium levels > 5.2 mmol/L). Sodium levels in the serum of patients with acute GE have varied between (128-166) mmol/L and potassium between (2.1-7.8) mmol/L; the prevalence of children with acute GE with altered levels of electrolytes was 55.6% in case of sodium and 53.7% in case potassium. Serum sodium levels are enhanced when the body loses more water than electrolytes [41] and decrease when the body loses more water than sodium, especially in cases of severe diarrhea and vomiting. Signs of hyponatremia include headache, confusion and lethargy. High sodium level causes thirst, confusion and seizures, and hyperkalemia causes the dangerous arrhythmias or abnormal heart rhythms. Hypokalemia usually cause milder symptoms, such as muscle cramps, fatigue and constipation. Analysis of alkaline reserve to 99.3% in patients with acute gastroenteritis highlight values (8.0-21 mmol/L) below the minimum limit of the range of normal variation (22.0 mmol/L). These low values ECO_2 suggests metabolic acidosis associated with dehydration of children due to diarrhea and vomiting children. In suspected cases of dehydration > 10% is required intravenous administration of fluids. The prevalence of children with gastroduodenitis (GD) who presented changes in biochemical and hematological parameters ranged from 1 to 100% depending on the parameter investigated (table 2). Leukocytosis and lymphocytosis observed indicate the inflammation process or a possible infection with *Helicobacter pylori* [42]. For all diseases analyzed reports neutrophil / lymphocyte were relatively small as 1.76 in the case of AA, 2.76 AAPA, GE 1.37, 2.5 ML and 3.0 for GD (fig. 1), they are below the level reported by other authors [10, 12-16].

Conclusions

WBC, CRP, ESR, neutrophil and lymphocyte percentages have shown significant changes at more than 50% of the children hospitalized for abdominal pain with specific symptoms of AA, AAPA, GD, GE, or ML, which confirm the nature of the inflammatory and infectious diseases.

Hematological and biochemical parameters analyzed (WBC, CRP, ESR, GR, and L are not diagnostic criteria for abdominal diseases when considering their individual values, due to low specificity.

A the combination of CRP and WBC, with Neutrophil/ Lymphocyte ratio determine increased positive predictive value of diagnostic and can help in making decisions regarding the diagnosis of these diseases especially in cases of severe and those severe requiring surgery.

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References

1.MERSKEY, H., BOGDUK, N., Pain Terms, A Current List with Definitions and Notes on Usage, Second Edition, IASP Task Force on Taxonomy, Seattle, IASP Press, 1994, p. 209-214.
2.D'AGOSTINO, J., Common abdominal emergencies in children. Emerg Med Clin North Am. No. 20, 2002, p. 139-153.
3.GRANT, H.W., PARKER, M.C., WILSON, M.S., MENZIES, D., SUNDERLAND, G., THOMPSON, J.N., et al. Adhesions after abdominal surgery in children. J. Pediatr. Surg., No. 43, 2008, p.152-156.
4.PELTOLA, H., AHLQVIST, J., RAPOLA, J., RASANEN, J., LOUHIMO, I., SAARINEN, M., ESKOLA, J. C-reactive protein compared with white blood cell count and erythrocyte sedimentation rate in the diagnosis of acute appendicitis in children. Acta Chir. Scand., No. 152, 1986, p. 55-58.
5.ERIKSSON, B., ARNBERG, H., OBERG, K., HELLMAN, U., LUNDQVIST, G., WERNSTEDT, C. & WILANDER, E. Chromogranins -new sensitive markers for neuroendocrine tumors. Acta Oncologica, No. 28, 1989, p. 325-329.
6.GRONROOS, J.M., GRONROOS, P., Leukocyte and C-reactive protein in the diagnosis of acute appendicitis. Br. J. Surg., No. 86, 1999, p.501-504.
7.PAAJANEN, H., MANSIKKA, A., LAATO, M., KETTUNEN, J., KOSTIAINEN, S., Are serum inflammatory markers age dependent in acute appendicitis? Journal of the American College of Surgeons, No. 184 (3), 1997, p. 303-308.
8.HALLAN, S., ASBERG, A., EDNA, T.H, Additional value of biochemical tests in suspected acute appendicitis. Eur. J. Surg., No. 163, 1997, p. 533-538.
9.YAZICI, M., OZKISACIK, S., OZFAN, M.O., GÜRSOY, H. Neutrophyl/ Lymphocite ratio in the diagnosis of childhood appendicitis. Turk J. Pediatric, No. 52, 2010, p. 400-403.
10.AL-ABED, Y.A., ALOBAID, N., MYINT, F. Markers de diagnosis in appendicitis acute. Am. J. Surg., No. 209(6), 2015, p. 1043-1047.
11.MYERS P. SURGICAL. In: Pathology of the appendix and its surgical treatment. Edited by: Williams R.A., Myers P., Chapman and Hall Medical, 1984, p. 137-141.
12.GOODMAN, D.A., GOODMAN, C.B., MONK, J.S. Use of the neutrophil:lymphocyte ratio in the diagnosis of appendicitis. Am. Surg., No. 61, 1995, p. 257-259, London.
13.KIM-CHOY, NG AND SHIH-WEI, LAI. Clinical analysis of the related factors in acute appendicitis. Yale J. Biol. Med., 2002, 75(1), p. 41-45.
14.ISHIZUKA, M., KITA, J., SHIMODA, M., ROKKAKU, K., KATO, M., SAWADA, T., et al. Systemic inflammatory response predicts postoperative outcome in patients with liver metastases from colorectal cancer. J. Surg .Oncol., No. 100, 2009, p. 38-42.
15.AL-KHAYAL, KA, AL-OMRAN, MA. Computed tomography and ultrasonography in the diagnosis of equivocal acute appendicitis. A meta-analysis. Saudi Med. J., No. 28, 2007, p. 173-180.
16.HEVERHAGEN, J.T., PFESTROFF, K., HEVERHAGEN, A.E., KLOSE, K.J., KESSLER, K., SITTER H. Diagnostic accuracy of magnetic resonance imaging: a retrospective evaluation of patients with suspected appendicitis (diamond). J. Magn. Reason Imaging, No. 25, 2012, p. 617-623.
17.THOMSON, C., UNDERWOOD, M., DOOKERAN, K., LLOYD, D., BELL, P. Role of sequential Leukocyte count and CRP in the diagnosis of acute appendicitis. Br. J. Surg., No. 79, 1992, p. 822-824.
18.ANDERSSON, R.E. Meta-analysis of the clinical and laboratory diagnosis of acute appendicitis. Br. J. Surg., No. 91, 2004, p. 28-37.
19.SACK, U. et al. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. BMC Surgery, No. 6(1), 2006, p. 15.
20.YANG, H.R., WANG, Y.C., CHUNG, P.K., et al. Laboratory tests in patients with acute appendicitis. ANZ J. Surg., No. 76, 2006, p. 71-74.
21.BELTRAN M.A. et al. Predictive value of white blood cell count and C-reactive protein in children with appendicitis. J. Pediatr. Surg., No. 42(7), 2007, p. 1208-1214.
22.KWAN, Y. KAREN, ALAN, L. NAGER, M.D. Diagnosing pediatric appendicitis: usefulness of laboratory markers. American Journal of Emergency Medicine, No. 9, 2010, p. 1009-1015.
23.YOKOYAMA, S., TAKIFUJI, K., HOTTA, T., MATSUDA, K., NASU, T., NAKAMORI, M., et al. C - reactive protein is an independent surgical indication marker for appendicitis: a retrospective study. World J. Emerg. Surg., No. 4, 2009, p. 36.
24.RODRIGUEZ-SANJUAN, J.C., MARTIN-PARRA, J.I., SECO, I., GARCIA-CASTRILLO, L., NARANJO, A. C-reactive protein and leukocyte count in the diagnosis of acute appendicitis in children. Dis. Colon. Rectum, NO. 42, 1999, p. 1325-1329.
25.GURLEYIK, E, GURLEYIK, G, UNALMISER, S. Accuracy of serum C-reactive protein measurements in diagnosis of acute appendicitis compared with surgeon's clinical impression. Dis Colon Rectum, No. 38, 1995, p. 1270–1274.
26.DAHL, M., VESTBO, J., LANGE, P., BOJESEN, S.E., TYBJAERG-HANSEN, A., NORDESTGAARD, B.G. C-reactive protein as a predictor of prognosis in chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med., No. 175, 2007, p. 250-255.
27.KAROUI, S., LAZ, S., SERGHINI, M., BIBANI, N., BOUBAKER, J., FILALI, A. Correlation of C-reactive protein with clinical and endoscopic activity in patients with ulcerative colitis. Dig. Dis. Sci., No. 56, 2011, p. 1801-1805.
28.KWAN, J. et.al. System infections after acute stroke. Aging Health, No. 491, 2008, p. 85-94.
29.ERYILMAZ, R., SAHIN, M., ALIMOGLU, O. The value of C- reactive protein and leukocyte count in preventing negative appendectomies. Ulus Treuma Derg., No. 713, 2001, p. 142-145.
30.STUART, J., WHICHER, J.T. Tests for determination and monitoring the acute phase response. Arch. Dis. Child., No. 63, 1988, p. 115-117.
31.HEINRICH, P.C., CASTELL, J.V., ANDUS, T. Interleukin-6 and the acute phase response. Biochem. J., No. 265, 1990, p. 621-636.
32.TOORENVLIET, B., VELLEKOOP, A., BAKKER, R., WIERSMA, F., MERTENS, B., MERKUS, J., et al. Clinical differentiation between acute appendicitis and acute mesenteric lymphadenitis in children. Eur. J. Pediatr. Surg., No. 21(2), 2011, p. 120-123.
33.KING, D., RAMACHANDRA, J., YEOMANSON, D. Lymphadenopathy in children, refers or reassure. Archives of disease in children. Education and practice edition, No. 99, 2014, p. 101-110.
34.LARSSON, L.O., BENTZON, M.W., BERG KELLY, K., et al. Palpable lymph nodes of the neck in Swedish schoolchildren. Acta Paediatr., No. 83(10) 1994, p. 1091-1094.
35.KANWAR VIKRAMJIT, S., RICHARD, H. SILLS. Lymphadenopathy. eMedicine. Eds. Gary J. Noel, et al., 2009.
36.GROSSMAN, M., SHIRAMIZU, B. Evaluation of lymphadenopathy in children. Curr. Opin. Pediatr. No 6(1), 1994, p. 68-76.
37.BLACK, R.E., COUSENS, S., JOHNSON, H.L., LAWN, J.E., RUDAN, I., BASSANI, D.G., et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet, No 375(9730), 2010, p. 1969-1987.
38.CADWGAN, A.M., WATSON, W.A., LAING, R.B., MACKENZIE, A.R., SMITH, C.C., DOUGLAS, J.G. Presenting clinical features and C-reactive protein in the prediction of a positive stool culture in patients with diarrhea. J. Infect., No. 41, 2000, p. 159-161.
39.BORGNOLO, G., BARBONE, F., GUIDOBALDI, G., OLIVO, G. C-reactive protein in viral and bacterial gastroenteritis in childhood. Acta Paediatr., No. 85, 1996, p. 670-674.
40.HSU TING-RONG, CHEN SHU-JEN, WU TZEE-CHUNG, RUEY-LUNG CHUNG, TANG REN-BIN. Tumor Necrosis Factor α and Interleukin-10 in Viral and Bacterial Gastroenteritis in Children. J. Chin. Med. Assoc., No. 68(6), 2005, p. 250-253.
41.CONLEY, SB. Hipernatremia. Pediatr. Clin. North. Am., No. 37(2), 1990, p.365-372.
42.BARBI, E., FALESCHINI, E., PELIZZO, G, MARTELLOSSI, S, ZENNARO, F, BUSSANI, R. Clinical quiz: Helicobacter pylori gastroduodenitis. J. Pediatr. Gastroenterol. Nutr., No. 41(1), 2005, p. 133-134.

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