

# Procalcitonin as the biomarker of inflammation in diagnostics of pediatric appendicitis and for prevention of unnecessary appendectomy

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## ABSTRACT

A total of 28 patients up to 15 years, who underwent appendectomy with preliminary diagnosis of acute appendicitis have been studied at M. Guramishvili Pediatric Clinic in 2004-2005 years. Procalcitonin concentration has been defined in patients' blood sera using the Immunoluminometric method (LUMITest PCT, BRAHMS Diagnostika, Berlin, Germany). Analysis of procalcitonin in different groups of patients has shown that increase in procalcitonin correlates with disease severity, and maximally increases in case of acute destructive appendicitis. The procalcitonin level can be used to confirm the diagnosis of acute appendicitis. It has been suggested that procalcitonin can be used not only as diagnostic marker for acute appendicitis but also as a prognostic marker of its complications. Using of procalcitonin in case of acute appendicitis would help to carry out timely surgical interventions and predict disease complications.

**KEYWORDS:** *procalcitonin, acute appendicitis, post operational complications*

**A**cute appendicitis still remains as one of the actual problems in children's urgent surgery. According to the data of the World Health Organization, in children 35-40% of operations have been carried out due to acute appendicitis. Noteworthy quantity of relaparotomy (0,8% in case of uncomplicated appendicitis and 6% in case of destructive appendicitis) carried out due to post operational complications [1] and high percent of unnecessary appendectomies –15-30% [2,3,4]. Absence of pathognomonic symptoms, great variability of clinical picture, frequency of atypical forms, difficulty in detection of local symptoms, often absence of changes in blood count, all of these factors make difficult to state diagnosis of acute appendicitis in children timely.

Although, investigations concerning the above-mentioned problem are plentiful, there are questions requiring explanation. One of the problems is the timely diagnostics of acute appendicitis and prevention of hyper diagnostics.

Investigations of procalcitonin, as one of the reliable biomarkers, in case of bacterial infections and traumas, have been carried out in the latest decade. Increasing of procalcitonin in blood sera in case of infections and inflammation was first described in 1993, as sepsis-induced protein in patients' serum with sepsis and bacterial infections [5]. According to its quantitative indices diagnostics of various bacterial infections and treatment strategy have been defined.

Concentration of procalcitonin selectively increases in case of bacterial infections, while in case of other infections (viral, autoimmune) its concentration remains normal [6,7,8]. Especially remarkable the rapid (after 2-4 hour from the beginning of the disease) increase of procalcitonin [9].

Interesting investigations have been carried out concerning the role of procalcitonin evaluation for diagnoses and prognosis of the post operational complications in case of various surgical pathologies (cardio surgery, abdominal surgery, orthopedics) [10,11]. It has been concluded that the level of procalcitonin correlates with severity of inflammation.

Owing to procalcitonin level we can differentiate infections of bacterial origin from nonbacterial inflammations, predict possible outcome of disease, possibility of post operational complications. All of these help physician to state diagnosis and make up therapeutic decision. The diagnostic value of procalcitonin's quantitative investigation exceeds such widely used parameters as fever, leukocyte count, erythrocytes' sedimentation rate.

There are few papers in pediatric surgery about the role of procalcitonin, as a biomarker of inflammation.

The aim of the study was quantitative analysis of procalcitonin, as an inflammatory biomarker, in children with acute appendicitis and prevention of unnecessary operational intervention.

## MATERIAL AND METHODS

A total of 28 patients up to 15 years, who underwent appendectomy with preliminary diagnosis of acute appendicitis (at M. Guramishvili Pediatric Clinic in 2004-2005 years) have been studied.

In these patients diagnosis of acute indefinite appendicitis (K35.9, ICD-10) and acute appendicitis with generalized peritonitis K35.0, ICD-10), were confirmed. The control group involved 8 healthy children with the age range 3-15 years.

Procalcitonin was investigated in laboratory of "Medical house-Testi". Procalcitonin concentration in patients' blood sera was defined using the immunoluminometric method (LUMITest PCT, BRAHMS Diagnostika, Berlin, Germany). Duration of test was two hours. Procalcitonin level range in healthy individuals was 0.1-0.2 ng/ml.

Morphological investigation of extirpated appendicitis has been carried out in Tbilisi Pathological Anatomy Scientific-practical Center for Adult and Children Pathology.

## RESULTS AND DISCUSSION

Have been investigated a total of 28 patients with the age range 3-15 years of both sex. Majority of patients were above 10 years (Tab.1).

Age	Boy		Girl	
	N	%	N	%
3-5 year	2	7.14	0	0
5-10 year	7	25	5	17.8
Above 10 year	8	28.57	6	21.4
Total	17	60.71%	11	39.29%

**Tab.1** Distribution of patients according to the age and sex

Patients were divided into three groups. The group I involved 5 patients where after appendectomy the diagnosis of acute appendectomy was not confirmed morphologically; the group II involved 12 patients with morphologically confirmed diagnosis of acute indefinite, uncomplicated appendicitis; the group III involved 11 patients with morphologically confirmed diagnosis of destructive form of acute appendicitis complicated with peritonitis (Tab.2).

Clinical diagnosis	Morphological diagnosis			
	Acute uncomplicated appendicitis		Acute destructive appendicitis	
	N	%	N	%
Acute appendicitis	12	42.85	11	39.28

**Tab.2** Distribution of patients according to the clinical and morphological diagnoses.

According to the results of the white blood count has been revealed that in the group I, three patients (60%) had moderate leukocytosis and two (40%) - the left shift in white blood count. At the same time level of procalcitonin in patients was not statistically changed compared to the

normal value and consisted  $0.17 \pm 0.04$  ng/ml (in the control group  $0.11 \pm 0.05$ ).

The moderate leukocytosis and left shift was detected in 6 patients (50%) in the group II and in 5 patients (45.5%) in the group III.

In patients with confirmed acute appendicitis (in the II and III group patients) the level of procalcitonin was above the normal value ( $0.71 \pm 0.28$  ng/ml).

In case of acute uncomplicated appendicitis (Group II) the level of procalcitonin was high ( $0.62 \pm 0.17$  ng/ml) and difference in comparison with the control group was statistically significant ( $p < 0.05$ ).

In patients with destructive form of appendicitis, complicated with peritonitis (Group III), level of procalcitonin was  $0.90 \pm 0.28$  ng/ml, that was significantly higher (table 3) in comparison with the control ( $p < 0.001$ ) and group II ( $p < 0.05$ ).

Thus, analysis of procalcitonin in different groups of patients has shown that increase in procalcitonin level correlates with disease severity, statistically and significantly differs between the groups and maximally increases in case of acute destructive appendicitis (Fig.1).

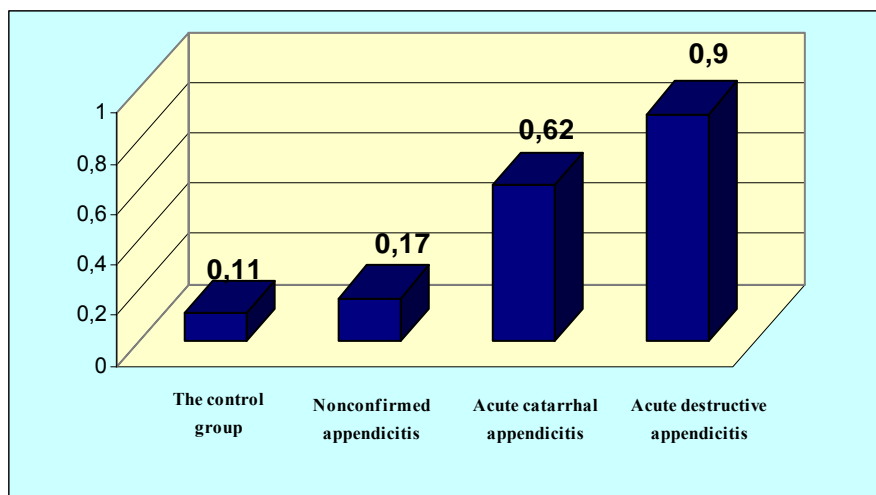
Proceeding from the aforesaid, when procalcitonin does not exceed the normal value, despite of certain clinical-laboratory data (pain in ileocecal region, slightly expressed peritoneal signs, leukocytosis, or the left shift in white blood count), there is no need in surgery, but when procalcitonin value exceeds the norm, in the presence of corresponding clinical symptoms (defans, Blumberg's sign, etc.) even if there are no changes in blood count, we should expect pathological changes in abdominal cavity. The higher procalcitonin level is the deeper and more profound disorders are expected.

Procalcitonin not only increases and confirms the diagnostic information, but also provides additional information independently from other clinical data.

Clinical forms	Leukocytes' total number		Leukogram		Procalcitonin		
	Increased	Normal value	Increased	Normal value	Increased	Normal value	Index
The control group	1 12.5%	7 87.5%	2 25%	6 75%	0	8 100%	$0.12 \pm 0.05$
The group I (unconfirmed appendicitis)	3 60%	2 40%	2 40%	3 60%	0	5 100%	$0.17 \pm 0.04$
The group II (acute uncomplicated appendicitis)	7 58.33%	5 41.66%	9 81.8%	2 18.2%	12 100%	0	$0.62 \pm 0.17$ $P_{1-2} < 0.05$
The group III (acute destructive appendicitis)	5 45.45%	6 54.54%	6 54.54%	5 45.45%	11 100%	0	$0.90 \pm 0.28$ $P_{1-3} < 0.08$

Notice: P-statistically significant difference between II and III group compared to the I (control) group.

**Tab.3** White blood count and procalcitonin in case of different clinical forms of acute appendicitis.



**Fig.1** Procalcitonin in case of different forms of appendicitis.

## DISCUSSION

Most of consultations in children's surgery are related to acute appendicitis. In almost 30% of cases, the acute appendicitis has so called atypical course that makes difficult to state diagnosis timely, which delays surgical intervention. We should take into consideration necessity of differential diagnosis as well, because in children's age many diseases are characterized by severe pain of lower abdomen. Moreover, nowadays we have no laboratory parameters that could indicate or reliably point on presence of acute appendicitis.

Proceeding from the aforesaid, investigation of markers, increase of which could indicate presence of appendix's acute inflammation and severity of its disorder would be of great value. Thus, importance of the above-mentioned investigation is absolutely clear.

The role of C-reactive protein in surgery has been studied in latest years [2,12]. One more possible diagnostic parameter of surgical pathology is the plasma protein – procalcitonin. Today, increase of procalcitonin is considered as the marker of bacterial infections.

We have shown on relatively small number of patients (28 patents) that procalcitonin is the good diagnostic marker of acute pediatric appendicitis and reliable marker for evaluation of its severity.

Importance of procalcitonin as nonspecific marker of inflammation has been stated in case of various bacterial infections, sepsis, septic shock, acute pancreatitis [6,8,13,14]. At the same time, procalcitonin as the biomarker of different surgical diseases has been discussed only in few papers, where have shown its importance as an indicator of post operational complications in case of cardio-surgical interventions [15].

Investigation of procalcitonin in 130 patients on second day after operations (aseptic operations, small surgical

operations, thoracotomies, large abdominal surgical interventions, cardio surgical operations) have shown that in some patients with high level of procalcitonin despite of satisfactory post operational state, in most cases the post operational complications (insufficiency of anastomosis, various purulent complications) were displayed [11]. It has been concluded that procalcitonin could be used as the diagnostic parameter providing monitoring of post operational complications. However, in other investigations, where 233 patients with acute appendicitis were studied, the diagnostic value of procalcitonin has not been stated [16].

At the same time in investigations carried out by Kouame et all. (70 pediatric patients) have been shown importance of procalcitonin as a good indicator of gravity of acute appendicitis, however its predictable role in diagnostics of acute pediatric appendicitis has not been proved [10].

Of course, we understand that our investigations have not been carried out on large amount of patients. The results would have been more reliable if it had been carried out in more patients, but anyway, we can conclude that procalcitonin can be used not only as diagnostic marker for acute appendicitis but also as prognostic marker of it complications. Using this marker in case of acute appendicitis would help us to carry out timely and indispensable surgical interventions and predict disease complications.

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## **Роль прокальцитонина, как биологического маркера, в диагностике острого аппендицита и исключения необязательных аппендэктомий у детей**

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### **Р Е З Ю М Е**

Обследовано 28 пациентов в возрасте до 15 лет, госпитализированных в педиатрическую клинику им. М. Гурамишвили г. Тбилиси в 2004-2005 г.г. и прооперированных с предварительным диагнозом – острый аппендицит. Анализ прокальцитонина проводился в плазме крови больного методом иммунолюминиметрии (LUMITest PCT, BRANMS Diagnostika, Berlin, Germany). Установлено повышение уровня прокальцитонина при остром аппендиците коррелирующее с характером морфологических изменений аппендикса: его уровень оказался выше при деструктивных формах аппендицита. Таким образом, прокальцитонин можно расценить не только как диагностический маркер при остром аппендиците у детей, но и как прогностический – с точки зрения возможных постоперационных осложнений. Показатель прокальцитонина в крови пациента с предварительным диагнозом острый аппендицит позволяет осуществить своевременную хирургическую интервенцию, прогнозируя возможность развития постоперативных осложнений.

**Ключевые слова:** , прокальцитонин, острый аппендицит, постоперационные осложнения