

UDC 616.98:579.842.23-036.2(477.54)

## CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF YERSINIOSES IN KHARKIV REGION

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Yersiniosis are one of the most common zoonotic infectious diseases. Registration of this diseases in Ukraine began from 1986. Kharkiv region is area with relatively high morbidity (0,59-2,4 on 100000 population) [1]. The most evidential method of diagnostics is culture, but grows of *Yersinia spp.* on common media is very bad. Indirect hemagglutination test (IHAT), which has high sensitivity, is still more common in Ukraine. Immunoferment analysis (IFA), polymerase chain reaction, immunoblot analysis are more specific and modern, but rather expensive and require specialized laboratory equipment and staff [2,3].

Despite great success in diagnostics of infectious diseases and development of new laboratory methods, vast majority of cases are not diagnosed or registered as different diagnosis. It connected with polymorphism of clinical signs and difficulty of specific diagnostics.

**Aim** – to improve yersiniosis diagnostics on the basis of clinical and laboratory data.

**Materials and methods** The object of the study were 61 patients with yersiniosis who were treated in the Kharkiv Regional Clinical Infectious Diseases Hospital during five years. From them 36 were men and 25 women. Age of the patients ranged from 18 to 85 years.

The diagnosis of yersiniosis in all patients was based on epidemiological, clinical, anamnestic data; results of additional laboratory studies which were in accordance with generally accepted clinical criteria. Complete blood count (CBC), urinalysis, coprocytogram, liver function test and stool culture was conducted for all patients. Final diagnosis was confirmed by results of serological studies (IHAT in pair serum with *Yersinia enterocolitica* 03, *Yersinia enterocolitica* 09 and *Yersinia pseudotuberculosis* antigen). For exclusion of viral hepatitis patients with jaundice were checked for anti-HAV IgM, HbsAg, and anti-HCV IgG by IFA. For determining the severity and clinical forms of the disease was used clinical and pathogenetic classification by N.D. Yushchuk et al. (1989) [5].

Statistical data processing was carried out by means of Statistica 6,0 software package. Comparative group analysis was performed by using  $\chi^2$  (Pearson) criterium. Differences with  $p < 0,05$  were considered statistically significant.

**Results and Discussion** Stool culture was negative in all cases. So, bacteriological diagnostics was not successful, that is comparable to other authors data [3,4]. According to IHAT in 69% cases were found

antibodies to *Y. enterocolitica* 03, in 10% – to *Y. enterocolitica* 09, in 2% – to *Y. pseudotuberculosis* in diagnostic titers. In other cases, the titer of antibodies to 03 and 09 *Yersinia spp.* was the same or did not reach the diagnostic values (in these cases the diagnosis was made on the basis of clinical and anamnestic, including epidemiological, data). Thus, from the 61 patients that were under our supervision, in 59 was diagnosed intestinal yersiniosis, in 2 – pseudotuberculosis. So, in the Kharkiv region *Y. enterocolitica* significantly more often was the reason of yersiniosis ( $p < 0,01$ ).

Men were sick more often than women ( $p < 0,05$ ).

According to age patients up to 50 years old were dominated (55 people, representing 90,16% of patients) ( $p < 0,05$ ). Among them prevailed patients from 21 to 30 years old (22 persons) ( $p < 0,05$ ). The average age of patients was  $29,32 \pm 14,1$  y.o.

Most of the patients were urban residents – 53 (86%).

There was no outbreaks. The incidence was recorded throughout the year in the form of sporadic cases.

Clinical diagnostics of yersiniosis was rather difficult due to lack of alertness by doctors. At prehospital period disease was suspected significantly rarely ( $p < 0,01$ ) – only in 8 (13,11%) patients. Other were sent to hospital with different diagnoses. More often patients entered hospital with diagnosis of acute intestinal infections (acute enterocolitis, gastroenterocolitis, gastroenteritis, food-borne toxicoinfection, salmonellosis) – 14 (22,95%) and acute respiratory infections, influenza – 12 (19,67%). In 8 (13,11%) cases preliminary diagnosis was fever of unknown origin, in 7 (11,48%) – viral hepatitis, in 4 (6,56%) – acute tonsillitis, in 3 (4,92%) – rubella, in 2 (3,28%) – leptospirosis, in 2 (3,28%) – infectious mononucleosis. One patient (1,64%) was hospitalized with suspicion on scarlet fever.

35 (57,38%) patients were hospitalized in the first week of illness, and only 8 (13,11%) of them – in the first three days (mainly patients with clinic of acute intestinal infection). Other patients – 24 (42,62%) – came to hospital in more late terms of the disease.

The severity of the disease in most cases was moderate (55,7%) or mild (32,8%). Severe disease was registered in 7 patients.

Cases with features of process generalization were dominated (46%); in 42% of patients – gastrointestinal form was recorded, in 12% – secondary-focal. But difference between generalized and gastrointestinal forms was not significant ( $p > 0,05$ ). These two forms significantly prevailed above secondary-focal ( $p < 0,01$ ). Abdominal form was not registered.

From anamnesis epidemica it was found that 11 (18,03%) patients connected the disease development with usage of vegetables (cabbage, carrots) and fruits (apples, strawberries), 3 (4,92%) associated disease with the consumption of raw milk, 3 (4,92%) – with usage of eggs. 8 (13,11%) patients indicated presence of rodents in their dwelling. Other could not specified any reason of the disease.

7 (11,48%) persons had the history of allergic reactions in the previous life.

Yersiniosis was recorded among different professional and social categories of people, but more often among students – 15 (24,59%) and unemployed – 20 (32,79%) ( $p < 0,01$ ).

Most patients – 39 (64%) – experienced acute onset of the disease; 22 (36%) – gradual. Intoxication syndrome prevailed in more cases. The first symptoms were fever, which was observed in 37 patients, in 31% of cases it was pyretic, in 21% it was accompanied by chills. General weakness was noticed by 27 persons, headache – 12, arthralgia – 7, aches – 4, muscle pain (especially in the calf muscles and neck) – 2. In the first day of the disease catarrhal syndrome was observed in 37,7% of patients. In 11 persons (18,03%) it was sore throat, in 7 (11,48%) – cough, mainly dry, in 5 (8,20%) – signs of rhinitis. Dyspeptic syndrome manifested with nausea (13,11%), vomiting (16,39%), loss of appetite (8,20%), flatulence (3,28%). 18 (30%) patients complained of loose stool (2-4 times daily), 12 (19,67%) – abdominal pain. 5 (8,20%) patients had pain in the lumbar region, 1 (1,6%) – dizuric disorders, 1 (1,6%) noticed dark urine. The rash at first day was observed in 3 patients.

Thus, at initial period significantly ( $p < 0,05$ ) predominated symptoms of intoxication, gastrointestinal and respiratory syndromes. Moreover fever incidence was dominant ( $p < 0,01$ ); difference between occurrence of gastrointestinal and respiratory tract affection was insignificant ( $p > 0,05$ ). Possibly this was the reason of misdiagnoses and this way prevalent preliminary diagnoses were acute intestinal and acute respiratory infections.

Climax period was characterized by considerable polymorphism. One of the most constant symptom was fever which was observed in 56 (91%) patients, and in 32 (52,5%) of them body temperature reached high numbers; in 19 (31,15%) it was febrile, in 5 (8,19%) – subfebrile and 5 (8,19%) – normal. The average duration of the fever was 10,858,87 days. Preferably incorrect (31%) and permanent (26%) types of temperature curves were observed. Less often met febris remittent (4,92%) and hectic (1,64%). Combination of different types of temperature curves also was present. In 25 (40,98%) patients fever accompanied by chills, in 93,44% – general weakness.

Arthralgic syndrome was observed in 19 (31,15%) patients and manifested as arthralgias (mainly pain in the knee, ankle, elbow, wrist joints, joints of hands and feet was marked). Arthritis symptoms were revealed rare. Some patients recorded pain and limited mobility in the joints (4,92%), swelling of periarticular tissues (8,19%), joints pain under palpation (3,28%), morning stiffness (1,64%).

In 27 (44,26%) patients rash was observed. It appeared on the first (32,79%) or second week (9,83%) of illness. Mainly it was small spots or roseolas – in 16 persons; rare – papular, maculo-papular, erythematous, hemorrhagic elements were found. In 7 (11,48%) patients rash was accompanied by skin itching. Favorite rash localization was abdomen, chest, back, upper and lower

extremities; in some cases the rash was most prominent in the natural folds and the flexor surfaces (4,92%), above the joints (6,56%). 4 (6,56%) patients experienced "socks" symptom, and 1 (1,64%) – "gloves". Exanthema duration was  $5,2 \pm 3,9$  days. At 8,19% cases disappearance of the rash accompanied by the appearance of skin peeling.

Approximately half of the patients (49,18%) experienced catarrhal symptoms like sore throat, dry cough, runny nose. On objective examination hyperemia of the soft palatum, palatal arches and uvula was identified in 57,38% of patients; enlargement of posterior pharyngeal wall follicles – in 22,95%; signs or follicular or lacunar tonsillitis – in 11,48%.

Quite regularly gastrointestinal and abdominal syndromes were observed. In 2/3 of patients a reduction or complete loss of appetite was noted; in 29 (47,54%) – nausea; in 22 (36%) – vomiting. Half of the patients complained of abdominal pain (often cramping, spasmodic; sometimes – of gnawing, cutting character). The pain preferentially localized in epigastric region (21,31%), right upper hypocondrium (14,75%), near umbilicus (9,84%) or was without clear localization (13,11%). On palpation abdominal pain also mainly was revealed in the epigastric region (45,16%), right upper hypocondrium (38,7%), right iliac region (32,26%) and periumbilical (35,48%) area. In 4 (6,56%) patients intestinal rumbling was noted. 37 (60,66%) patients had infrequent (3 – 5 times per day) loose stool, often without pathological admixtures (only 7 patients noticed mucus and 1 – blood in feces).

In most patients signs of reticuloendothelial system affection were revealed. Lymphadenopathy was present in 28 (45,9%) patients. More often it was involvement to the pathological process of angle- and submandibular lymph nodes – in 24 (39,34%) persons, cervical – in 18 (29,51%), axillary – in 12 (19,67%). Enlargement of auricular, occipital, inguinal lymph nodes was observed in some patients. 1/3 of patients had polylymphadenopathy. Splenomegaly was found (mainly by percussion) in 18,03% patients. Spleen was enlarged on average by 1 cm (0,5 to 2 cm). Authentically more often (in 41 patients) hepatomegaly was revealed ( $p < 0,01$ ). Liver size was increased by an average of 1,6 cm (0,5 to 4 cm). Complaints on dark urine in 7 (11,5%) patients and pain in the right upper quadrant in 9 (15%) also reflected affection of hepatobiliary system. On examination in 16 (26%) patients yellowness of sclera was determined; in 10 patients it was short-term duration (1-2 days). Jaundice of the skin was observed in 9 (15%) patients; it appeared in the period from 4<sup>th</sup> to 13<sup>th</sup> day of the disease and was of brief duration ( $7 \pm 5,15$  days).

5 (8,20%) patients had neurological symptoms like seizures, neck stiffness, upper extremities paresthesias. 3 (4,92%) patients experienced signs of toxic shock.

Urinary tract and kidneys also were involved in the pathological process. 14 (22,95%) patients had complaints on back pain, 2 (3,28%) – on frequent and difficulty urination. Positive or doubtful Pasternatsky sign was revealed in 16,39% of cases.

So, in climax period authentically predominant symptoms were fever, hepatomegaly, hyperemia of the soft palatum, palatal arches and uvula, diarrhea ( $p < 0,01$ ). Rather often polylymphadenopathy, rash and arthralgia were revealed, but rare then mentioned above ( $p < 0,05$ ).

Also in climax period compared to initial we saw a significant increase in the occurrence of next symptoms: fever, headache, loss of appetite, nausea, vomiting, diarrhea, arthralgia ( $p < 0,01$ ). Significantly more often ( $p < 0,01$ ) rash was revealed. Detection of some objective data like hepatomegaly, polylymphadenopathy, yellowness of sclera also was helpful in making a diagnosis.

In CBC of 17 (28%) patients signs of anemia were defined. Moderate leukocytosis was revealed only in 32 (52,46%) patients, in 2 (3,28%) persons leukopenia was observed, in 18 (30%) – relative lymphopenia. Shift to the left in leukocyte formula was revealed in 23 (38%) of patients, increased ESR – in 41 (67%). So, leukocytosis, shift to the left in leukocyte formula and increased ESR were present significantly more often ( $p < 0,01$ ). Diagnostic value of these three indicators was similar ( $p > 0,05$ ).

Changes in biochemical liver function tests were recorded in 21% of patients. Mainly it was signs of mild cytolytic syndrome – increased alanine aminotransferase (ALT) was revealed in 14 patients (ALT in average was  $2,18 \pm 1,36$  mmol/l); mesenchymal-inflammatory – increased thymol test (an average of 11 units) was detected in 6 persons; cholestatic syndrome – total bilirubin was increased in 6 patients (in 3 of them direct fraction prevailed, in 3 – indirect). Moderate decrease of sublimat (in average  $1,64 \pm 0,36$  ml) detected in 8 patients. The difference between the occurrence of syndromes was unreliable ( $p > 0,05$ ).

Urine test showed only signs of toxic irritation of the kidneys (leucocyturia, microhematuria, slight proteinuria) in 1/3 of patients.

So, clinic of yersiniosis was characterized by polymorphism. In infectious hospital patients with generalized and gastrointestinal forms mainly were treated. Patients with other forms possibly were treated by rheumatologists, surgeons, traumatologists and other specialists with different diagnosis.

All cases with polymorphic clinic, which include signs of intoxication, gastrointestinal tract involvement combined with respiratory appearances or hepato- (rare hepatosplenomegaly), polylymphadenopathy, rash, arthralgias should be suspicious for yersiniosis and specific laboratory methods, including IFA and PCR (as addition to stool culture and IHAT), should be prescribed to reveal real situation about incidence of disease, improve the diagnostics and further treatment.

**Conclusions** 1. In the Kharkiv region intestinal yersiniosis prevailed above pseudotuberculosis. The main causative agent is *Y. enterocolitica* O3.

2. Disease was registered as sporadic cases, that occurred throughout the year. Male persons of working age were mainly affected.

3. The clinic of yersiniosis was characterized by pronounced polymorphism, which lead to difficulties in diagnosis. About half of patients had signs of process generalization.

4. Specific laboratory methods, including IFA and PCR (as addition to stool culture and IHAT), should be prescribed to reveal real situation about incidence of disease, improve the diagnostics and further treatment.

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**Results and Discussion** From the 61 patients that were under our supervision, in 59 was diagnosed intestinal yersiniosis, in 2 – pseudotuberculosis. Patients up to 50 years old were dominated. The incidence was recorded throughout the year in the form of sporadic cases. The severity of the disease in most cases was moderate (55,7%) or mild (32,8%). Severe disease was registered in 7 patients. Generalized (46%) and gastrointestinal (42%) forms dominated. Most patients – 39 (64%) – experienced acute onset of the disease. Climax period was characterized by considerable polymorphism. Intoxication syndrome was predominant. Catarrhal, gastrointestinal and abdominal syndromes, hepatomegaly, polylymphadenopathy and rash were observed often enough. Arthralgic syndrome, splenomegaly, kidney affection were revealed less frequently.

**Conclusions** 1. In the Kharkiv region intestinal yersiniosis prevailed above pseudotuberculosis. The main causative agent is *Y. enterocolitica* O3. 2. Disease was registered as sporadic cases, that occurred throughout the year. Male persons of working age were mainly affected. 3. The clinic of yersiniosis was characterized by pronounced polymorphism, which lead to difficulties in diagnosis. About half of patients had signs of process generalization. 4. Specific laboratory methods, including IFA and PCR (as addition to stool culture and IHAT), should be prescribed to reveal real situation about incidence of disease, improve the diagnostics and further treatment.

**Key words:** yersiniosis, clinical, epidemiological data