THE FEATURES OF ACUTE BRUCELLOSIS IN AZERBAIJAN REPUBLIC

Huseynov Elchin Mammad oglu
Department of Infectious Diseases
Azerbaijan Medical University
23 Bakikhanov str., district Narimanovsky, Baku, Azerbaijan, AZ1022
elchinhuseynov@mail.ru

Abstract

It is well known, that the injury of organs and systems and also immunological rates considerably determine clinical course and the result of brucellosis. In the article are presented the results of examination of 120 patients with acute brucellosis. The control group included 30 practically healthy persons. Groups were representative by the age and sex. The diagnosis of brucellosis was set on the base of complaints, anamnesis, epidemiological and clinical data and the results of serological examination of the blood. All patients also underwent the fixation of interleukin-6, iinterleukin-4 and TLR-2 in the blood serum. The detailed epidemiological, clinical and immunological characteristic of patients with brucellosis was presented. Among examined persons prevailed men, persons of young able-bodied persons and rural dwellers. It was revealed, that the dominating way of transmission was the contact one. The highest level of infection was fixed among the workers of farm enterprises and veterinarians. The season features were also revealed, the highest level of morbidity was in summer-autumn period. The main clinical features were: fever, arthralgia, risen disposition to perspire, hepatosplenomegaly. It was revealed, that the level of pro-inflammatory interleukins considerably prevailed over the level of anti-inflammatory ones. Despite the high sensitivity of PCR diagnostics, the positive results in our research were received only in one third of patients.

Keywords: acute brucellosis, interleukin-4, interleukin-6, toll-like receptors, immunoglobulin.

1. Introduction

Epidemiological and epizootic situation with brucellosis in the world remains rather strained for today, so this infectious disease remains a complicated and topical socio-economic problem for many countries. According to the data of Associated committee of experts of WHO (1986), this disease is registered in animals in 155 countries of the world. Brucellosis is most spread in the countries of Mediterranean, Asia Minor, South and South-Eastern Asia, Africa, Central and Southern America [1–3].

In last decades epidemiological situation with brucellosis in Azerbaijan Republic remains unfavorable and is characterized with epizooties of brucellosis among farming animals – small and big cattle that are the main source of brucellosis causative agent for humans [4–6]. The important social aspect is the high specific weight of children teenagers and persona of active working age among patients with brucellosis and also involvement of people who are not professionally connected with the source of possible infection in epidemiological process [7, 8]. This disease flows with injury of all organs and systems that leads to the extremely unfavorable results: disablement and invalidism of patients that determines its high socio-economic significance [9]. Alongside with it brucellosis is characterized with the imbalance of cellular and humoral immunity. It is attended by the decrease of the indices of T- and B-cellular link of immunity that results in activation of immunoglobulin (A,M,G) and essential disorders of cytokine regulation as the increase of pro-inflammatory cytokines (IL-1β, IL-6) and TLR-2 [10, 11]. The excessive TLR activation and production of uncontrolled quantity of pro-inflammatory cytokines can favor the development of systemic inflammatory reaction, further injury of tissue, formation of complications of the main disease [12]. That is why the important value is inherent not only to the features of epidemic process, clinical course and early diagnostics of this pathology but also the study of immunological rates that allows prognosticate the severity of disease and choose the adequate pharmacotherapy.

2. Aim of research

To study the features of acute brucellosis among patients of Azerbaijan republic taking into account epidemiological and clinical-immunological rates.

3. Materials and methods of research

We examined 120 persons with acute brucellosis, who were on the stationary treatment at infectious clinic of Baku city. The mean age of patients was 35,9±2,8 years. Men prevailed among patients – 75,3 %. The control group included 30 practically healthy persons. Groups were representative by the age and sex.

The diagnosis of brucellosis was set on the base of complaints, anamnesis, epidemiological and clinical data and the results of serological examination of the blood (determination of IgM and IgG by ELISA method). All patients also underwent the fixation of interleukin-6, iinterleukin-4 and TLR-2 (CD282) in the blood serum.

The content of interleukin-6 (IL-6) in the blood serum was fixed by ELISA method using the set "Human IL-6 Platinum ELISA" (Bender MedSystems, Austria). The content of interleukin-4 (IL-4) in the blood serum was fixed by immune-enzyme method using the standard set of "IL-4 ELISA" by "Diaclone", France. The content of toll-like receptors TLR-2 (CD282) in the blood serum was fixed by immune-enzyme analysis using the set "TLR-2 (CD282) Human ELISA Kit" (Abcam, England).

Statistical analysis of the received results was carried out using "STATISTICA 6,0" using parametric and non-parametric methods of assessment of the received results.

The criteria of inclusion in the research were the following: patients with acute brucellosis, with disease duration up to 3 month and with positive serologic reactions and/or positive PCR.

4. Results of research

To study the features of epidemiology of acute brucellosis among population, there were used the data of 120 patients, who were on the stationary treatment during 2013–2015. Among the examined persons prevailed rural dwellers – 81,67 % (**Fig. 1**).
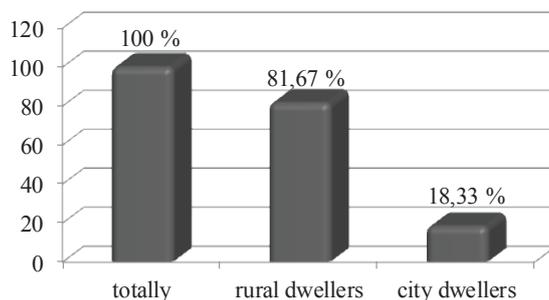

Fig. 1. Distribution of patients with brucellosis by the dwelling place

Among patients prevailed men – 75,3 % and persons of the young active working age. The structure of patients with brucellosis was divided by age as following: 18–29 years – 34,17 %, 30–39 years – 30,83 %, 40–49 years – 17,5 %, 50–59 years – 16,67 %, 60–69 years – 0,83 % (**Fig. 2**).
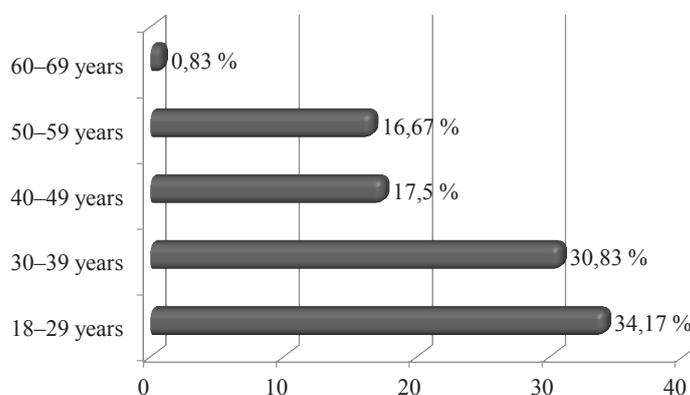

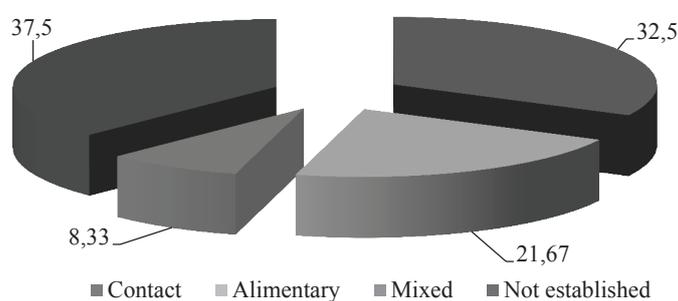**Fig. 2.** Distribution of patients with brucellosis depending on age

Having studied the professional activity of patients, it was established, that 46,67 % dealt with animal husbandry. The highest level of infection was fixed among the workers of farm enterprises and veterinarians. The persons, whose activity was not connected with care of animals, were 45 % (**Table 1**).

Table 1

Distribution of patients with brucellosis depending on the type of activity

Profession	Patients with brucellosis (n=120)	
	Abs.	**%**
Farmer	27	22,5
Housewife	21	17,5
Student	5	4,17
Pensioner	2	1,67
Clerk	7	5,83
Veterinarian	29	24,17
Medical worker	6	5,0
Cook	9	7,5
Unemployed	4	3,33
Data are absent	10	8,33

The main way of infection was the contact one in 32,4 % of cases, in 21,9 % – alimentary, in 8,2 % – mixed. In 37,5 % of patients the source and way of infection transmission was not established (**Fig. 3**).

37,5   32,5   8,33   21,67

■ Contact ■ Alimentary ■ Mixed ■ Not established

Fig. 3. Distribution of patients with brucellosis depending on the way of transmission

At the analysis of season features of brucellosis it was revealed, that the most part of patients with brucellosis was registered in summer and autumn comparing with the spring-winter period (**Fig. 4**).

The main clinical manifestations of acute brucellosis were: fever with rigor – in 100 % of patients, arthralgia – in 64,2 % persons, risen disposition to perspire – in 70 %, raise of lymph nodes in – 43,3 %, hepatosplenomegaly was revealed in 74,2 % of patients (**Table 2**).

Table 2

The main clinical features in patients with acute brucellosis

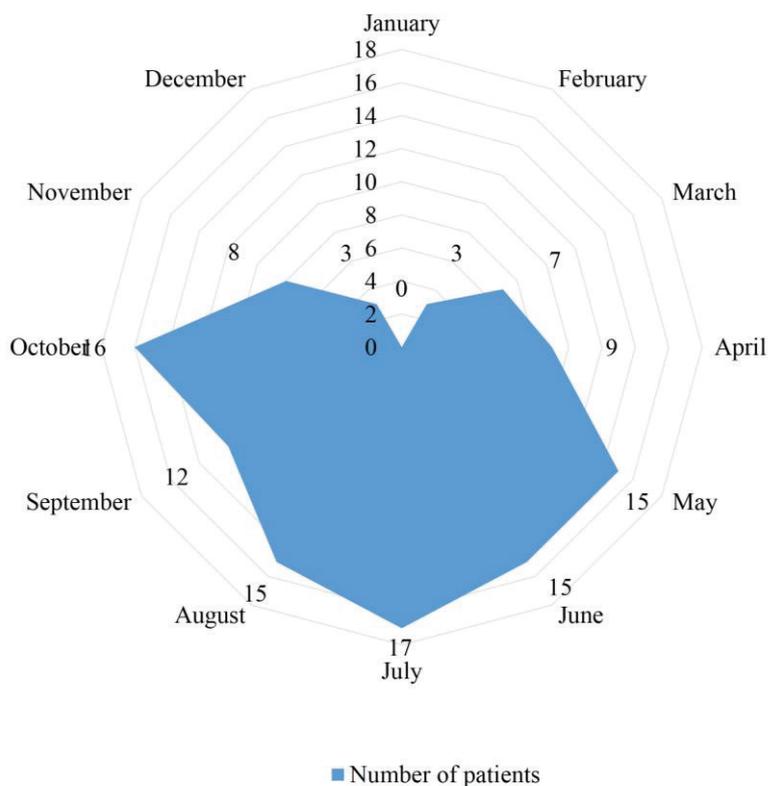| Clinical manifestations	Patients with acute brucellosis (Abs.)	Patients with acute brucellosis (%)
General weakness	105	87,5
Fever with rigor	120	100
Disposition to perspire	84	70
Arthralgia	77	64,2
Lymphoadenopathy	52	43,3
Hepatosplenomegaly	89	74,2

Fig. 4. Distribution of patients with brucellosis depending on season

At objective examination anemia, deafness of heart tones, hypotonia, dysfunction of digestive organs (anorexia, stomach ache, coated tongue), increase of liver and peripheral lymphatic nodes were observed more often.

At PCR for revelation of brucel, the positive reaction was established only in 34,2 % (**Fig. 5**).
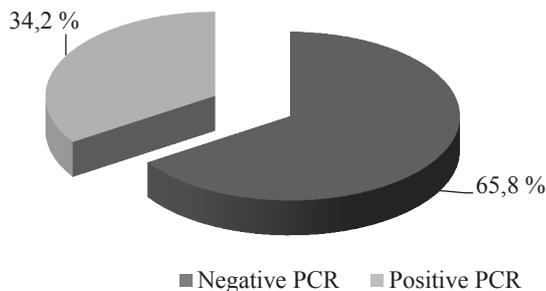

Fig. 5. Distribution of patients with brucellosis depending on PCR result

It was established, that the level of interleukin-6 in the blood serum of patients with acute brucellosis was 15,29±1,43 pg/ml, interleukin-4 – 11,30±0,71 pg/ml, and level of TLR-2 – 6286±349 pg/ml (**Table 3**).

Table 3

Indices of IL-6, IL-4 and TLR-2 in patients with acute brucellosis

Indices	Patients with acute brucellosis (n=120)	Healthy persons (n=31)
IL-6, pg/ml	15,29±1,43	7,63±0,41*
IL-4, pg/ml	11,30±0,71	16,58±0,94*
TLR-2, pg/ml	6286±349	2982±230*

*Note: * p<0,05 – the difference is reliable comparing with the control group*

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It was revealed, that the levels of interleukin-6 and TLR-2 were 2 and 2,1 times more in patients with acute brucellosis comparing with the control group, respectively. Whereas the level of interleukin-4 was on the contrary 1,5 times less comparing with healthy persons.

5. Discussion of the results of research

In the works of Zheludkov M. M. and co-authors (2004, 2005, 2009) was grounded the universality of enzyme-linked immunosorbent assay (ELISA) usage for the laboratory diagnostics of brucellosis in epidemiological and clinical practice that allows reveal the brucellosis antigen and specific antibodies of the different classes of immunoglobulin.The determination of the level of specific IgG, IgA, IgM allows judge about the intensity of infectious process, probability of repeated infection, character of local inflammatory changes of bone-articulate system that finally favors the improvement of diagnostics and quality of the treatment [13, 14].

The authors also established the high diagnostic effectiveness of polymerase chain reaction (PCR) at brucellosis infection, which use in epidemiological practice allowed determine the infection of people in the different centers of infection much more often than the traditional methods of serological diagnostics. At that the positive result in PCR has a practical importance only at presence of clinical signs of disease by the possibilities of determination of brucels DNA in persons, who have a contact with the living vaccine strains, excreted by the vaccinated animals in external environment. This fact must be taken into account at interpretation of the positive results of this reaction [14, 15]. In our research at PCR for revelation of brucel the positive reaction was established only in 34,2 %.

In patients from ecologically unfavorable region the polylymphoadenopathy, articulate syndrome with early formation of arthritis and involvement of many joints in pathological process were observed more often, hepatomegaly was observed less often. On this background the negative or questionable reactions of agglutination were detected with the high probability, in patients with typical clinical course the high titre of specific antibodies was revealed seldom that generally indicate the low immune reactivity of organism [16–18], that proves our data.

The evolution of brucellosis in the modern conditions takes place as an increase of frequency of acute brucellosis with early development of focal metastatic and infectious-allergic injuries that worsen the clinical course that testifies to the early development of sensitization in patients already in acute phase of brucellosis process [19]. Alongside with it more early injuries of locomotor apparatus are observed (in first 2–3 months after the beginning of disease) and also more frequent injury of vessels (scleritis, conjunctivitis, positive symptom of tourniquet and other) that is explained by the authors also by the early allergic rebuilding of the organism [20]. The arthralgic syndrome was observed in our patients in 64,2 %.

The study of clinical-immunological rates at acute brucellosis demonstrated that in the mechanism of development of pathogenesis of brucellosis the important role is played by immunological disorders that can be presented as following: at coming into organism the brucels multiply and old cells die, endotoxin is released at their splitting and the macrophages and lymphocytes throw out pro-inflammatory cytokines as the response to it that is testified by the risen level of IL-1β and IL-6, and the production of anti-inflammatory cytokines: IL-4, IL-10 increases as the response to it. At the same time with received data the decrease of IF −γ concentration was revealed that undoubtedly influences the system of phagocytosis, lowering its functional activity and does not provide the full elimination of causative agent from the organism [4].

6. Conclusions

1. Among patients with acute brucellosis the diagnosis was proved by PCR method only in 34,2 % of persons.

2. At acute brucellosis the significant changes in immunological rates were revealed as statistically significant raise of pro-inflammatory IL-6, TLR-2 and decrease of anti-inflammatory IL-4 that testifies to the development of inflammatory process.

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