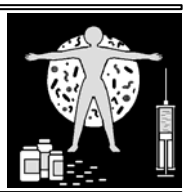
# INFECTIOUS DISEASES



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## ANALYSIS OF DEATH CASES OF HIV-INFECTED BASING ON THE MATERIALS OF SPECIALIZED DEPARTMENT

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We analyzed the deaths of HIV-infected basing on materials of SHI (state health care institution) Novgorod Regional Infectious Diseases Hospital during 2004-2010. The main cause of death was generalized tuberculosis, chronic viral hepatitis in cirrhotic stage, late admission. Social disadapted individuals (patients with chronic alcoholism and drug users) who were not registered in dispensary have prevailed among the dead.

***Keywords: HIV infection, analysis of death cases, chronic viral hepatitis, tuberculosis***

В работе проведен анализ летальных исходов ВИЧ-инфицированных по материалам по материалам ГУЗ «Новгородская областная инфекционная больница» за 2004-2010 гг. Основной причиной смерти больных являлись: генерализованный туберкулез, хронический вирусный гепатит в цирротической стадии, позднее поступление. Среди умерших преобладали социально дезадаптированные лица (больные хроническим алкоголизмом и наркопотребители) не состоявшие на диспансерном учете.

***Ключевые слова: ВИЧ-инфекция, анализ летальных исходов, хронический вирусный гепатит, туберкулез***

Mortality rate among HIV-positive people continues to grow. 73 959 patients with HIV infection, including in 2009 — 13,990 people [1-3] have died for various reasons in the Russian Federation.

Velikiy Novgorod is one of the cities with relatively affluent incidence rates of HIV infection. 1,348 HIV-infected patients have been registered at the end of the 2010.

It is worth to mention increase of mortality among HIV-infected people against the background of stabilization of indicators of primary detectability.

Analysis of death causes in patients with HIV infection is relevant not only for clinicians but also for public health organizers as the level of mortality from advanced stages of disease caused by HIV reflects the level of medical care to such patients.

*The goal of the research.* Analysis of the causes of death in patients receiving treatment in specialized department for the past seven years.

### Materials and methods

We have carried out retrospective analysis of patients who died with diagnosis of HIV infection for the period 2004-2010. The results and outcomes of treatment of 698 patients in specialized department of SHI Novgorod Regional Infectious Diseases Hospital have been analyzed. Analysis of autopsies has been carried out basing on findings of pathoanatomical protocols. Group for research included both patients with previously known HIV status and patients with newly diagnosed HIV infection during hospitalization.

### Results and discussion

High percentage of socially disadapted individuals (patients with chronic alcoholism and drug users) who were not registered in dispensary has been noted among the observed group of patients (Table 1).

Table 1

Social status of deceased patients with HIV infection in the period 2004-2010

| Social status | Absolute numbers | % |
|---|---|---|
| Employed | 6 | 12.8 |
| Not employed | 15 | 31.9 |
| Persons without permanent residence | 1 | 2.12 |
| Addicts | 21 | 44.7 |
| Suffering from chronic alcoholism | 2 | 4.25 |
| Disabled persons | 2 | 4.25 |

743 patients with diagnosis of HIV infection has been treated during analyzed period in the hospital. 47 patients died, among them 68.1% had AIDS, total mortality was 6.23%.

The greatest number of deaths among both men and women has been registered in the age group of 20-39 years: males — 89.3%, women — 89.5%. The number of deaths in men exceeded the number of deaths in women in 1.47 times reflecting the general statistical tends (Table 2).

Table 2

Deceased patients by gender and age

| Age/Gender | Male | % | Female | % |
|---|---|---|---|---|
| 20-29 | 12 | 25.5 | 10 | 21.3 |
| 30-39 | 13 | 27.7 | 7 | 14.9 |
| 40-49 | 3 | 6.38 | 2 | 4.25 |
| More than 50 | — | — | — | — |
| Total | 28 (59.6%) | | 19 (40.4%) | |

When analyzing the clinical stage of patients who were taken under medical observation for the first time, manifest of disease has been revealed; this indicates the

duration of disease and late admission of patients for medical care [4]. As a consequence, the growth of mortality has been noted (Table 3) among HIV-infected patients in the stage of AIDS. Over the entire period of observation 47 patients with HIV infection have died in the hospital, it was 36.2% patients only in 2010.

Table 3

The relative number of death cases

| Year / Patients | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|---|---|
| Relative number of death cases | 0 | 8,51 | 12,8 | 14,9 | 12,8 | 14,9 | 36,2 |

More than 95% of deaths with AIDS are caused by severe manifestations of secondary diseases (mainly AIDS-associated diseases and tumors).

Currently there is a tendency in the Russian Federation to increase of patients surviving to advanced stages of HIV infection without being on the follow-up, and in most cases they were unaware of their HIV status and, accordingly, did not receive preventive treatment for opportunistic disease and antiretroviral therapy.

It is known that HIV-infected patients have the lower level of CD4 cells and thus the greater number of infections that develop on the background of the underlying disease.

The structure of secondary diseases in patients with HIV infection varies in the Russian Federation. Most of them are tuberculosis, cytomegalovirus infection, cerebral toxoplasmosis, severe forms of candidosis, herpetic infections. Prevention, diagnosis and treatment of secondary diseases are important components of the complex health care. Prevention of secondary diseases in HIV-infected patients is carried out as the primary prophylaxis — before development of these lesions (preventive therapy appointed on the basis of epidemiological, clinical and immunological parameters), and secondary prophylaxis - to prevent recurrence after treatment.

Analysis of deaths showed that the half per cent of deaths were due to opportunistic infections (Table 4).

Table 4

Causes of death in patients with HIV infection in 2004-2010

| Death cause | Absolute numbers | % |
|---|---|---|
| Generalized tuberculosis | 11 | 23,4 |
| Pneumocystis pneumonia | 4 | 8,51 |
| Meningoencephalitis | — | — |
| Toxoplasmosis of brain | 2 | 4,25 |
| Meningoencephalitis unspecified etiology | 1 | 2,13 |
| Non-Hodgkin's lymphoma | — | — |
| Cytomegalovirus infection | 1 | 2,13 |
| Generalized herpetic infection | 1 | 2,13 |
| Kaposi's sarcoma | 1 | 2,13 |
| Angiogenic sepsis | 7 | 14,9 |
| Viral hepatitis in cirrhotic stage | 10 | 21,3 |
| Bacterial complications | 9 | 19,4 |

Of all analyzed cases antiretroviral therapy has been taken by 2.13% of patients. Moreover, therapy was initiated against the backdrop of critically low level of CD4 cells. It is known that the success of initiated therapy is directly proportional to the number of CD4 cells. 6 people themselves have stopped therapy due to lack of commitment, or treatment was withdrawn because of side effects of drugs, and also because of using narcotics. The main reasons for low coverage of HAART in patients with HIV from the analyzed group were antisocial behavior, reluctance to go to medical facilities and changing lifestyles, even in cases where patients were aware of their illness. None of analyzed patients received prophylaxis from AIDS-associated diseases, which is indicator of shortcomings in the organization of dispensary observation and management of such patients.

Every year there is an increasing number of late diagnosed patients who come to hospital in serious and critical condition in Novgorod and in other cities with the diagnosis of HIV infection established few days before death (Table 5). The diagnosis of HIV infection was established during last hospitalization in 12.8% of patients.

Table 5

Late diagnosed cases of HIV infection among hospitalized patients

| Year / Patients | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|---|---|---|
| Late diagnsed cases | — | — | — | — | 1 | — | 6 |

The term «late diagnosed cases of HIV infection» includes newly diagnosed HIV infection in patients with clinical AIDS and / or with the level of CD4 lymphocytes below 350 cells / uL. Patients with this diagnosis represent a serious challenge to the health system. Their treatment is more costly and less effective [5].

Only 6.38% of patients from all of analyzed group were on regular dispensary at the Center for AIDS. Low level of dispensary observation of patients is explained by psychological features of such category of patients and shortcomings in the organization of medical care for people with low social level.

Analyzing the causes of death in patients with HIV / AIDS, we have identified the diseases which were observed most frequently: chronic viral hepatitis in the stage of decompensation, angiogenic sepsis, and generalized tuberculosis. Patients came to hospital in serious condition. Most of these deaths occurred in the first 7-10 days of admission. Among death causes significantly more often patients had chronic viral hepatitis in cirrhotic stage in comparison with other causes of death ($p > 0.05$). Associated diseases in HIV-infected most frequently were chronic viral hepatitis in the stage of cirrhosis — in 27.3%, bacterial complications — in 19.4%; angiogenic sepsis — in 14.9% and gastrointestinal candidosis (59.6%), which had been recurrent.

The high mortality rate was observed due to complications of chronic viral hepatitis in decompensated cirrhotic stage, especially in patients with AIDS with the

level of CD4-lymphocytes below 200 cells / uL. Deaths from viral liver cirrhosis were observed in the early stages of HIV infection, with CD4-lymphocyte level was above 200 cells / uL and fluctuated in wide range (from 200 to 500 cells / uL). Also, patients often had hepatitis C and hepatitis B + C as the accompanying diseases. When parenteral route of infection prevailed we odentified hepatitis C and hepatitis of mixed etiology: hepatitis B + C, hepatitis B + C + D. Viral hepatitis were distributed by etiological factor in the deceased patients as follows: chronic hepatitis C in 46.8% of patients, combination of chronic viral hepatitis C and B in 14.9%, combination of chronic viral hepatitis C, B, D in 4.25 %, chronic viral unidentified hepatitis in 2.13%. Consequently the majority of patients had viral hepatitis B and C. 31.2% of patients with chronic viral hepatitis disease had already had cirrhotic stage with ascites and other signs of portal hypertension. Clinical diagnosis of chronic hepatitis in cirrhotic stage was confirmed in all patients, not only in vivo, but also due to results of autopsies. The main causes of death were bleeding from varicose veins of the esophagus and stomach, ascites, peritonitis and other bacterial complications. Hepatic encephalopathy was continuously progressive or recurrent.

Tuberculosis is one of the most common opportunistic infections. Every year the number of TB patients increases on 2%. Currently tuberculosis is one of the leading causes of death in people infected with HIV [6].

It is known that HIV infection is a risk factor for developing of active tuberculosis in infected with Mycobacterium tuberculosis. Risk of tuberculosis in these patients increases with increasing immunosuppression. It is known that in persons infected with HIV and Mycobacterium tuberculosis the annual probability of developing tuberculosis is about 10%, while in non-infected with HIV this probability is less than 10% throughout life.

According Rakhmanova A.G. in patients in early stages of HIV infection and during first 2 years of follow-up care TB has the same form and clinical manifestations that in patients who are not infected with HIV [7]. In the late stages generalized, disseminated TB with necrosis usually develops, it most often occurs with complications. Complexity of diagnosis of tuberculosis caused by immunodeficiency is explained by development of wide range of AIDS-associated infections and secondary diseases with rare detection of Mycobacterium tuberculosis in sputum of patients with HIV at late stage of the disease and often negative Mantoux test.

The share of patients who died from tuberculosis was 23.4%. These were patients from socially burdened groups: homeless people, active consumers of drugs. All of them arrived in hospital in stage of AIDS in severe condition and the complexity of TB diagnosis was due to the fact that these patients experienced AIDS-associated infections. It must be noted that the research contains the number of death cases from tuberculosis basing on data of specialized department not including the number of death cases of tuberculosis that were registered in TB dispensaries. Therefore, we can safely assume that the actual level of mortality from TB is much higher.

## Conclusions

1. Novgorod region has unfavorable situation concerning HIV epidemic, which is characterized by growth of deaths from opportunistic infections and comorbidity. Mortality rate tends to increase, despite the use of HAART in HIV-infected.

2. High mortality is mainly caused by the social characteristics of patients, most of who were infected using of narcotics.

3. The high percentage of socially disadapted persons who do not undergo the dispensary observation and do not receive antiretroviral therapy is still grows.

4. The main causes of death in patients with AIDS were generalized tuberculosis (23.4%), Pneumocystis pneumonia (8.51%), toxoplasmosis with brain lesions (2.7%), generalized form of CMV infection (2.13%), generalized herpetic infection (2.13%), Kaposi's sarcoma (2.13%).

5. The largest group of deaths (21.3%) consisted of patients with chronic viral hepatitis in cirrhotic stage. Causes of death for these patients were hemorrhage from varicose veins of the esophagus and stomach, erosive bleeding, ascites.

6. Angiogenic sepsis (14.9%) remains frequent cause of death in the hospital. These patients were active drug users and as a result treatment of pyosepticemia with etiotropic drugs was difficult and inefficient.

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