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Review Article

REVIEW ARTICLE

NOSOCOMIAL INFECTIONS IN INTENSIVE CARE UNIT: GLOBAL PROBLEM OF MODERN MEDICINE

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ABSTRACT.

Increased volume of surgical interventions, improvement of efficiency of special treatment modalities and modes of respiratory support, as well as development of new generation antibiotic medications has led to significant improvement of clinical outcomes of intensive therapy for critical conditions. At the same time, introduction of innovative and largely invasive interventions resulted in the emergence of new disease entities.

Presently, the development of hospital-acquired infections (HAI) has become one of the riveting and serious problems of modern hospitals. These infections often lead to prolonged hospital stay, which in turn adds to the morbidity and mortality, worsen patient quality of life and also has significant economic consequences [1-5].

There are number of varying definitions of infections related to medical care [6]. According to the WHO, infections that develop 48 hours after hospitalization, excluding the incubation period, are called hospital-acquired or nosocomial infections. Some authors also include here infections that develop 4 weeks after patient's discharge from hospital or 30 days after surgical interventions are also included in this category. Infections that develop within 30 days after last chemotherapy in patients with metastatic cancer are also included as additional criteria according to a medical literature [7]. Other authors conclude that readmission of patients with established infection that was the result of previous hospitalization as well as any infectious diseases of hospital employee that develops secondary to the work in the hospital, irrespective to the time of onset of symptoms (during or after the hospital visit or stay) shall also be regarded as the hospital-acquired infections (HAI) [8-10].

INTRODUCTION.

The average prevalence of HAI is around 3.5-10.5% or 9.0-91.7 cases per 1000 patient-days [11]. It is estimated that the probability of infectious complications increases after five days of hospitalization [12]. According to the modern medical knowledge, the prevalence of HAI of various causes among the hospitalized patients in North America and Europe is around 5-10% and those in Latin America and Asia is around 40% [13,14]. The mortality among patients with HAI is seven times higher than among other patients aligned based on age, sex, main disease and comorbidities and severity of disease. According to the official statistics, HAIs are fourth most common cause of mortality in the US leading to 90.000 deaths annually. Annual economic burden and additional costs associated with the treatment of HAIs in the US is about 2.4-4.5 billion US dollars [15-17].

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There are currently 30 various forms of HAIs. However, catheter-associated urinary tract infections (CAUTI), catheter related bloodstream infections (CRBSI), as well as ventilator associated pneumonia (VAP) are the most serious life-threatening device-associated infections [18,19].

According to several sources, there is no difference in distribution of HAI among intensive care units and various hospital wards [20]. However, majority of researchers believe that intensive care units represent the overall majority of hospital acquired infections [14,21-25]. Despite the continuous development of intensive therapy, the attributed mortality from hospital-acquired infectious complications in the intensive care units remains high. According to various authors it can be as high as 40% depending on the type of intensive care units [14,26-29]. It is important to underline the existing differences in the prevalence, prevalence and specificities of clinical development of HAI depending on character of main disease, type of hospital department and patient groups. Serious chronic comorbidities, prolonged hospitalization as well as expanded use of invasive devices, including respiratory support equipment, intravascular and bladder catheters are major risk factors for development of HAI among patients of somatic intensive care units [30]. At the same time the volume and character of surgical operation, need for full range of intensive therapy, including prolonged use of ventilation, total parenteral nutrition, blood transfusion therapy and several other factors impact the occurrence of hospital-acquired infections in intensive care units of surgical clinics. Additionally, the poor clearance of surgical infection sources that can become the source of secondary infection, sepsis, translocation of microbes in the GI tract and need for surgical revisions or take-backs are also risk factors for development of HAI [21]. Moreover, having prior medical treatment in different clinical departments of the same or other hospital puts the patients at additional risk of colonization with pathogenic bacteria that can become a source of HAI. These patients constitute a different group of interest.

According to one of the largest studies dedicated to the research of HAI (the EPIC study), the prevalence of HAI in general wards of developed countries is estimated as 5-15%, while it is about 20.6% in the intensive care units [31,32]. Also, in exceptional instances it approaches 50%, EPIC study also reported the prevalence of HAI in Eastern Europe and England as 23,0-23,5% [33-35], and in the low and middle income countries as 35,2% [4].

As it is seen from above, there is a significant difference in prevalence of HAI in various countries of the world [14,22,24,36-38,39,40]. And these differences are partially attributed to the level of country's overall development. The similar situation is observed with prevalence of various types of HAIs, related to use of invasive devices.

The study conducted among 55 intensive care units in eight countries of the world showed that prevalence of HAI attributed to the use of invasive devices as about 22.5 cases per 1000 patient-days [41]. The results of multicenter study in Argentina [42] and research done in cancer and neurology clinics in Brazil [43] and Turkey [44] demonstrated the prevalence of HAI as 80 cases per 1000 patient days. In European studies the prevalence varied significantly, ranging from 1.7-44.7 cases per 1000 catheter-days and 1.4-23.0 cases per 1000 catheter-days to 3.2-56.9 cases per 1000 ventilation-days [41,42], which is somewhat different from prevalence reported by NNIS/NHSN for US clinics [45,46].

However, the prevalence of HAI associated with invasive devices in developing countries is 2-8 times higher than in the US and Germany with higher prevalence of VAP [48] as per

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reports for US by NHSN for period until 2008 [45,46] and by Germany's Krankenhaus-Infektions-Surveillance-System (KISS) for period until 2009 [47], Recent report by International Nosocomial Infection Control Consortium for period of 2007-2012 developed based on data from 503 intensive care units in developing countries also demonstrated the prevalence of VAP to be 15 times higher and catheter-associated infections of urinary tract 4 times higher than in economically developed countries [49].

The problem of HAI associated with the use of invasive devices in low income countries is not well studied [50]. However according to analysis of performance of intensive care units in developing countries for the period of 2002 through 2005, the prevalence of these infections were 14.7% or 22.5 cases per 1000 patient-days in intensive care units. It is important to note that VAP was recognized as leading pathology (41% out of all infection cases associated with invasive devices or 24.1 per 1000 ventilation days). Catheter-associated infections of blood stream comprised of 30% of all infections associated with invasive devices and constituted 12.5 cases per 1000 catheter-days, making them second most prevalent. Catheter-associated infections of urinary tract constituting 29% of device-associated infections or 8.9 cases per 1000 catheter-days were third most prevalent. The mortality associated with catheter-associated infections is reported to be 35.2%, while VAP associated mortality is 44.9% [41]. The same authors later reported the prevalence of device-associated infections in 36 developing countries of Latin America, Asia, Africa and Europe for period of 2004-2009 and compared this data with the one reported in the INICC final document. Both reports demonstrated the "leading position" of VAP in comparison with catheter-associated infections of urinary tract and catheter-associated infections of blood stream, respectively 14.7 and 15.8 cases per 1000 ventilation-days [51]. Similar results were demonstrated in the papers from China [52], Libia [53], and Cuba [54], where the INICC methodology was also used

The data on prevalence of HAI in Asia is limited. The nation-wide monitoring of HAI is performed only in few developed countries of Asia, including Taiwan, Singapor, Japan and South Korea [55,56],

Several studies on prevalence of HAI in South Asia have reported the prevalence of HAI in intensive care units to be as high as 20 cases per 1000 patient-days in intensive care units [57,58]. However the prevalence of VAP is reported as 14,7/1000 ventilation-days, catheter-associated infections of bloodstream – 4,7/1000 catheter-days, and of catheter-associated infections of urinary tract - 8,9/1000 catheter-days [59,60]. According to these studies the attributed mortality of patients due to infectious complications ranges from 7% to 46%. Out of that 6,5% - is mortality related to device-associated HAI, 14% - catheter-associated infections of bloodstream. The 30-day mortality of 46% of patients was related to VAP [61]. At the same time, the length of hospitalization was extended to 10-17 days, and economic burden was estimated as high as 865-13.000 USD [62,63]. Based on the results of this and several reports from other developing countries, it is estimated that prevalence of HAI associated with invasive devices are 10-20 times higher than in the US as presented in the latest report by US National Health Safety Network [19,64]. Therefore, even in the era of «patient safety» there is a significant gap between the US and developing countries.

One of the main reasons for high prevalence of HAI in developing countries is inadequate hygienic conditions, poor infrastructure, overload of intensive care units, lack of human resources, as well as lack of

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appropriate knowledge, differences in standards of care and in implementation of preventive and infection eradication programs, prolonged and inappropriate use of invasive dvices, irrational use of antibiotic therapy [4,65].

Unfortunately, there are no similar data to describe the situation in Azerbaijan Republic. Available publications are sporadic and do not reflect the real situation with prevalence of HAI in the country's hospitals. There are several reasons explaining this current situation, including the low level of experience in data collection and modern methods of data interpretation, as well as lack of professional personnel and funding. Implementation and expanded use of standardized definitions are often limited by poor reliability of microbiological data and other diagnostic procedures, lack of special computer software and data to monitor the HAI throughout the country given the differences in overall development level of various regions of country, as well as lack of national guidelines on this topic.

The purpose of presenting the data on prevalence of HAI in the world here is not only to demonstrate the differences in the prevalence of HAI based on the country's level of development, including economic and healthcare system. It is also important to show the differences in character and prevalence level of various types of HAI in the intensive care units. These differences are partly explained by specifics of the hospital wards and patient groups that are mostly cared for.

The level of healthcare system development and quality of medical care can explain these differences. However, there are other possible causes for the differences in morbidity level, including the methodological quality of conducted research and discrepancy in criteria for confirmation of HAI diagnosis. We believe that variation in definitions and precise formulations of diagnosis as well as in data collection methodology also contribute to the variation of obtained results.

According to data presented by various authors, in several countries the prevalence of HAI is ten times higher than officially reported. This discrepancy is believed to be partly related to poor registration of HAI cases and in some circumstances it is secondary to non-reporting of HAI cases [66,67]. Unfortunately, such a shortsighted policy of hospital wards along with lack of universal control system can lead to serious negative consequences. Therefore, summarizing the above-mentioned, it is important to conclude that availability of precise statistical data on prevalence of, as well as morbidity and mortality associated with HAIs has to become the integrated part of healthcare institution's performance analysis.

The concerning statistics related to prevalence of HAI requires the open sharing of official data on infection cases associated with hospital stay, at least on selected types of HAIs [27,68]. Active interventions by relevant agencies enabled to change the definition of HAIs from the group of unavoidable complications to the preventable ones. This fact helped to adopt appropriate legislation on mandatory registration of several types of HAI and on refusal by insurance companies to reimburse hospitals for the expenses related to the treatment of these infections [69]. At the same time, according to several sources, there is no evidence that strict implementation of mandatory registration procedures can lead to decrease in incidences of HAIs [70,71].

Unfortunately, the lack of universal monitoring, diagnosis and registration of HAI as well as absence of feedback with clinicians leads to incorrect reflection of real situation about

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HAI.

The data by International Consortium on HAI Control [72] and of two systematic reviews [73], on prevalence of HAI confirm both the high risk of such complications and the underestimation of seriousness of the problem.

Despite the fact that HAI are considered that most prevalent secondary complications threatening the safety of patients globally, the lack of data reflecting the real prevalence of HAI at national and regional levels, including in the resource-limited settings, prevents the correct appreciation of global nature of this problem. In countries where less than 5% of gross domestic product is spent for healthcare and where the workforce estimation is less than 5 per 1000 people, other serious problems of healthcare become priority [74]. Information gap is also related to the lack of experience among government agencies in infection control, including the organization of joint work to collect, analyze and interpret the data.

Monitoring and control over prevalence of HAI is one of the priority areas for healthcare systems in developed countries. One of its components is the establishment of committees to control the HAI in each clinic. The committees nowadays shall be responsible for identification and registration of HAI, implementation of educational programs to prevent the appearance of new cases and spread of infection as well as organization of standardized preventive measures, as well as to identify the level of resistance to particular antibiotic therapies, development of detailed description of antibacterial medications, limiting the use of particular group of antibacterial medications and implementation of clinical protocols on user of rational antibiotic therapy.

As it is described above, the absence of universally accepted criteria for HAI diagnosis creates the collision in the work of and communication between the committees and clinicians and epidemiologists in relation to prevalence of HAIs.

The development of modern definitions of HAI in the US was initiated within the framework of Comprehensive Hospital Infections Project (CHIP) in 1969-1972 and National Nosocomial Infections Study (NNIS) in 1970-1974. Currently, the criteria of CDC (NHSN) are most widely used ones [75]. However, difficulty, subjectivity, labor intensity as well as expensiveness and lack of sensitivity of definitions provided by CDC, prevent their use in comparative analysis of prevalence indicators of HAI within single clinic and/or among various institutions.

The differences in criteria used to make a diagnosis of HAI in various countries also create some difficulties in this regard. Therefore the development and adoption of clear criteria for diagnosis of HAI with the purpose to prevent over diagnosis or underestimation of current situation would be one of the main objectives for national agencies on control over and prevention of HAI.

Nevertheless, despite the significant efforts and expenses required for effective epidemiological monitoring of HAI, about 1/3 of true infections remain unregistered. Presently, special modules, statistic programs and templates for identification, registration and reporting of data on prevalence of HAI in hospitals are gaining the popularity [76]. However, they have certain limitations, such as: not all available tools are easy to understand and not easy to implement, the registration in some hospitals is performed by nursing staff which may not consider certain specifics, the specialist of infection control committee do not always participate in the data collection, people involved in the process do not always have necessary skills and knowledge of statistical analysis. At the end this makes the analysis of collected data more difficult.

This led to need for development of alternative strategies for control and prevention of HAI. The development of algorithms, including electronic medical records and HAI

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related risk stratification in the hospitals is regarded as most important one. Automated monitoring algorithms that use the presented data independently or along with the results of microbiological analysis, increase the sensitivity and objectiveness of monitoring, and also decrease the financial expenses and are less labor intense [77]. On the other side, the mandatory use of clinical signs in addition to laboratory criteria for formulation of final diagnosis of any type of HAI (complete clinical and microbiological definition by CDC) requires an in-depth analysis and more time consuming.

Although the implementation of automated algorithms is limited due to lack of funding, the mandatory use of coding for HAIs shall become the integrated part of process to ensure the control over HAI. However, even such an approach has its limitations that may lead to discrepancies in final diagnosis. One of the researches demonstrated the discrepancy between the prevalence of HAI provided by healthcare administration and specialists of clinic departments of hospital, when former underestimated the prevalence of HAI and wrongly reported zero prevalence of VAP among severely ill patients of surgical and trauma departments [78].

Other article demonstrated the lack of correlation between primary data and final diagnosis, including in particular the lack of sensitivity and specificity in diagnostic codes of bloodstream infections [79]. VAP is the most complex pathology to verify the diagnosis. Along with catheter-associated infections of bloodstream, the diagnosis of VAP cannot be verified based solely on the data from microbiological studies as it can lead to underestimation or over diagnosis of this particular clinical entity [80]. Attempts to include the data from radiological examinations into final report also led to high numbers of false positives and low prognostic value of such approach [81]. At the same time, the different strategy that included the combination of radiologic data and use of antibiotic therapy had higher sensitivity (81%) and higher prognostic value (100%) [82]. Similar attempts were made in regards to catheter-associated infections of urinary tract [83].

So, the data obtained from various researches demonstrates that HAI represent the serious and at the same time hidden problem of healthcare.

Given the above-mentioned, the complete reporting on incidence, morbidity and mortality secondary to HAI shall become the part of mandatory evaluation of performance of any healthcare institution. And here the following mandatory items that need to be included: adoption of criteria for diagnosis of HAI, registration of all cases of HAI and daily use of commonly accepted and locally adapted recommendations on prevention and treatment of HAI.

It is impractical to use the results of large multicenter studies in the work of particular medical organizations. Specificities of clinics and certain limitations, including lack of human resources and technical capacity, type of intensive care units, patients groups as well as availability of dynamic data on level of antibiotic resistance shall be considered during the conduction of end point analysis.

The problem discussed here is indeed multidisciplinary and thus requires well organized and joint work of all interested hospital departments, joint decision making, protocols for adequate modern empiric antibiotic therapy, interventions to decrease the level of resistance to antibiotics, decrease in length of hospitalization and mortality level.

Having complete knowledge about prevalence of HAI, about local pathogens and conduction of regular monitoring of antibiotic resistance can ensure the highly effective control of HAI in any given hospital ward. It can also help to optimize the antimicrobial therapy and as the end-point it can lead to the improved clinical

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outcomes and overall care process andd as such wil lead to decreased financial burden of medical institutions.

Improvement of quality and efficiency of organizations responsible for epidemiological control of HAI, registration and mandatory reporting of HAI to designated agencies will decrease the prevalence of HAI and improve the clinical outcomes. Adaptation of standardized clinical protocols and definitions that are based on clinical data and also evaluation of their prognostic value in comparison with currently used international definitions is of paramount importance.

Use of standardized criteria for verification of HAI diagnosis based on recommendations of WHO (or others) will ensure the correlation of data and comparability of outcomes during the development and conduction of comparative research on prevalence of HAI between the countries**.**

There is a need for improvement of research methodology used to evaluate the prevalence of HAI, including the standardization of criteria for verification of diagnosis of HAI as well as for development of modern web resources and publicly available reports on prevalence of HAI in the hospitals that will help to achieve the expanded outreach [84]. There is a need for additional efforts to improve the policy and programs targeting the prevention and control of infections, including the development of scientific and clinical collaborative networks among healthcare institutions within the country.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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ETHICAL APPROVAL

No ethical approval was required as this was a clinical case.

CONSENT

Patient permission was obtained prior to writing this report.

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