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ARTIFICIAL VENTILATION AS A RISK FACTOR CAUSING HOSPITAL-ACQUIRED PNEUMONIA (HAP) IN PATIENTS TREATED IN THE INTENSIVE CARE UNIT OF A CARDIAC SURGERY HOSPITAL

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Hospital-acquired pneumonia (HAP) is the most common purulent septic infection among patients treated in intensive care units (ICUs) at cardiac surgery hospitals. Risk factors that can cause HAP, in particular, contribution made by artificial ventilation (AV) have not been studied enough. Our objective was to examine an epidemiological role played by AV in HAP occurrence among children and adults treated in the intensive care unit at a cardiac surgery hospital. We examined health records of 5318 patients (503 children and 4815 adults) who had a cardiac surgery due to congenital heart diseases or acquired cardiovascular disorders over 1 year. HAP was identified according to the epidemiological standards for case definition. Besides, we took into account pre-nosologic HAP cases, that is, patients already having certain pathological symptoms typical for purulent septic infections, but still, even combined, these symptoms were not enough to diagnose a typical HAP case in accordance with the standard case definition. Data were statistically analyzed by calculating the χ^2 goodness-of-fit test. We established that most HAP cases occurred among patients of a cardiac surgery hospital who were being treated in the intensive care unit after a surgery. We proved AV to be the leading risk factor causing HAP. Higher incidence rates of HAP were detected among children in comparison with adults. We showed that Klebsiella pneumoniae was the primary infectious agent that caused HAP. Particularly, background respiratory diseases and diseases of the central nervous system were proven to be endogenous risk factors of developing HAP among patients treated in the ICU at a cardiac surgery hospital.

Key words: *cardiac surgery hospital, intensive care unit, hospital-acquired pneumonia, risk groups, etiology, role played by artificial ventilation.*

Intensive care units (ICUs) are those divisions in medical organizations where there are the highest risks of hospital acquired purulent septic infections [1, 2]. Hospital acquired pneumonia (HAP) is the most common infection among patients treated in them [3, 4]. HAP occurs in 9–65 % patients in intensive care units [5–7], *Klebsiella pneumoniae* [8] being the leading infectious agent.

HAP in intensive care units often occurs in patients who have to undergo artificial ventilation (AV). In this case it is conventional to call it AV-associated or ventilator-associated pneumonia (VAP) [2, 7, 9]. Artificial airways created with an AV device are assumed to make swallowing less efficient. Bacteria can penetrate the lower airways either directly or through a split between tracheal tube walls and

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the airways thus causing an infection. Besides, long-term ventilation creates elevated risks of infections in the airways due to humidifiers and ventilation circuits [7].

Incidence of ventilator-associated pneumonia varies from 5 to 80 % (depending on a population of patients, severity of their cases, and AV duration) [10]. Frequency of occurring HAP is close to 80–100 % after a two-week AV period. Stratified incidence rate of HAP varies from 9.1 to 52.7 per 1000 AV-days spent in an ICU [10–12].

There are some works that dwell on results produced by comparative assessment of HAP incidence among children and adults. Some authors state that adults, especially those who are older than 60 years, have ventilator-associated pneumonia more often than children [13]. But at the same time others note there are no differences in incidence rate of the disease among children and adults [14].

There are available literature data on frequency of ventilator-associated pneumonia and risk factors that cause the disease in ICUs of surgical, oncologic, neurological, therapeutic and pediatric in-patient hospitals [5, 15]. But the issue hasn't been given proper attention with respect to an intensive care unit of a cardiac surgery hospital.

Our objective was to examine an epidemiological role played by artificial ventilation in occurrence of hospital acquired pneumonia among children and adults treated in an intensive care unit of a cardiac surgery hospital.

Materials and methods. Our study was accomplished in a specialized cardiac surgery hospital for children and adults where open heart surgeries and endovascular invasions on the heart and vessels are performed. Surgeries are performed in equipped operating rooms; then, patients are moved into an ICU where they can spent some time, starting from 1 day and for a longer period, depending on their clinical condition. After that patients are moved into cardiac surgery units. Patients who have undergone an endovascular invasion can be moved directly into an ordinary surgery unit without any time spent in an ICU.

We examined health records of 5318 patients (503 children and 4815 adults) who were treated in a cardiac surgery hospital and who had a heart surgery due to congenital heart diseases or acquired cardiovascular disorders over the last year. HAP was identified in accordance with the epidemiologic standard for the case definition [16]. Besides, we took into account pre-nosologic HAP, that is, cases when patients already had certain pathological symptoms typical for pneumonia but all these symptoms combined still were not enough to diagnose typical pneumonia according to the standard case definition [17]. Incidence rates of typical and prenosological HAP were calculated per 1000 patients. Our analysis included only patients who had HAP as a monoinfection. We considered a period during which a postoperative patient was ventilated starting from intubation and up to the first clinical signs of HAP as well as AV duration in case the first clinical HAP signs appeared after extubation. And in case a patient was ventilated several times during his or her period in the ICU, we took only a period of time from the next intubation and up to the first clinical signs of HAP. Ventilator-associated pneumonia was a HAP case when the disease occurred after a patient spent 48 hours ventilated [15]. HAP incidence density was calculated as per 1000 AV days.

We considered microorganisms to be isolated from patients with HAP only if they were identified at appearance of the first clinical HAP signs. Repeated cases of infectious agents' identification were neglected.

All materials were statistically analyzed by calculating χ^2 goodness-of-fit test. We determined confidence intervals for calculated rates (0.95 % CI) using WinPepi software package, Version 11.65 (created by Professor Joe Abramson, Israel). Differences between the rates were considered statistically significant at $\chi^2 \geq 3.8$ ($p < 0.05$). Assessment of risk factors involved calculating relative risk (*RR*) and respective 95 % confidence intervals.

Results and discussion. Overall, over the last year 503 children and 4815 adults

were operated in the examined cardiac surgery hospital. 246 children and 1567 adults were moved to the ICU after surgery. Data in Table 1 show that there were only sporadic HAP cases among patients who didn't spend any time in the ICU after surgery. Conversely, almost all HAP cases occurred among patients who were sent to the ICU after surgery and spent some time ventilated. A number of typical and prenosological HAP among patients treated in the ICU was greater among children (31.5 and 111.9 per 1000 accordingly) than among adults (16.6 and 47.2) (χ^2 = 7.5 and 40.3; p = 0.007 and 0.001 accordingly). Overall, incidence with both typical and prenosological HAP turned out to be by 2.2 times higher among children (143.4 per 1000) than among adults (63.8) (χ^2 = 219.9, p = 0.001).

Data in Table 2 indicate that incidence of typical and prenosological HAP turned out to be higher among children and adults who had a long AV period (632.7 and 301.6 per 1000 accordingly) than among those who had a shorter one (42.2 and 53.9 per 1000 accordingly), by 15.0 and 5.6 times (χ^2 = 12.2 and 62.1 accordingly, p = 0.001 in both cases). *RR* amounted to 14.9 (7.8–28.5) and 5.6 (3.6–8.6) accordingly. In case AV duration was shorter than 48 hours, there was no difference in incidence between children and adults (χ^2 = 0.6, p = 0.5); but if it was longer than 48 hours, than incidence among children was by 2.1 times higher than among adults (χ^2 = 21.8, p = 0.001). All these data indicate there is an epidemiological contribution made by AV into developing HAP in an ICU of a cardiac surgery hospital, especially among children.

Table 1

Incidence of hospital acquired pneumonia among patients in cardiac surgery hospital after heart surgery; both treated in the ICU and those who didn't spend any time there, cases/1000

Patients' group	Age	A number of patients	Typical HAP		Prenosological HAP cases		Total	
			Number of cases	cases/1000	Number of cases	cases/1000	Number of cases	cases/1000
Not treated in the ICU	children	217	0	0	0	0	0	0
	adults	3248	1	0.3 [0.01–1.7]	5	1.5 [0.5–3.5]	6	1.8 [0.7–4.0]
	total	3465	1	0.3 [0.01–1.6]	5	1.4 [0.5–5.3]	6	1.7 [0.6–3.7]
Treated in the ICU with some time spent on AV	children	286	9	31.5 [14.5–58.9]	32	111.9 [77.8–154.2]	41	143.4 [104.9–189.2]
	adults	1567	26	16.6 [10.9–24.2]	74	47.2 [37.3–58.9]	100	63.8 [52.2–77.1]
	total	1853	35	18.9 [13.2–26.1]	106	57.2 [47.1–68.7]	141	76.1 [64.4–89.1]

Table 2

Incidence of hospital acquired pneumonia among patients in cardiac surgery hospital after heart surgery who were treated in the ICU and had a short period (up to 48 hours) and longer period (more than 48 hours) spent on artificial ventilation, cases/1000

Age group	AV for less than 48 hours			AV for more than 48 hours		
	A number of patients	A number of HAP cases	per 1000	A number of patients	A number of HAP cases	per 1000
Children	237	10	42.2 [20.4–76.2]	49	31	632.7 [482.8–765.8]
Adults	1503	81	53.9 [43.0–66.5]	63	19	301.6 [192.3–430.2]
Total	1740	91	52.3 [44.5–67.1]	112	50	446.4 [355.9–547.7]

Table 3

The incidence density of typical and prenosological HAP among patients treated in the ICU (per 1000 AV days)

HAP clinical form	The incidence density	
	children	adults
Typical	45.0 [20.8–83.7]	24.8 [16.3–36.3]
Prenosological	108.1 [120.8–234.1]	68.7 [54.3–85.4]
Total	80.1 [58.3–107.4]	47.7 [38.5–57.0]

Having calculated stratified incidence rates, we established (Table 3) that the incidence density of typical and prenosological HAP per 1000 patient-days was by 1.8 and 1.6 times higher accordingly among children (45.0 and 108.1 accordingly) than among adults (24.8 and 68.7 accordingly) (χ^2 = 6.6 and 6.3 accordingly, p = 0.01 in both cases). Summated incidence of typical and prenosological HAP was by 1.5 times higher among children than among adults (χ^2 = 9.1, p = 0.003).

Sex-adjusted incidence assessment (Table 4) revealed that the epidemic process regarding all HAP forms was more intense among men than among women after a short period spent on AV (χ^2 = 15.9, p = 0.001). But in case AV was performed for more than 48 hours, incidence grew by 6.1 times among men and by 16.6 times among women (χ^2 = 95.5 and 13.3 accordingly, p = 0.001 in both cases). Ultimately incidence rates among men (432.8 per 1000) matched to those among women (466.6 per 1000) (χ^2 = 0.1, p = 0.7).

K. pneumoniae and fungi from *Candida* genus (Table 5) were most frequently isolated from phlegm of patients with typical or prenosological HAP. Detection rates for these microorganisms amounted to 17.7 and 15.5 per 100 examined patients accordingly. *S. aureus* и *P. aeruginosa* were detected less frequently, each microorganism in 7.3 % cases. There were no statistically significant differences in how often most agents were isolated from patients after either short-term or long-term AV, except *P. aeruginosa* and *K. pneumoniae*. We also detected a trend for increasing frequency of isolating *P. aeruginosa,* from 4.4 to 12.0 (χ^2 = 2.8, p = 0.1) and statistically significant growing in occurrence of *K. pneumoniae,* from 12.1 to 28.0 per 100 examined patients (χ^2 = 5.6, p = 0.02). Therefore, patients who spend less than 48 hours on AV are likely to get infected with *K. pneumoniae* due to endogenous reasons, and patients who spend more than 48 hours on AV, due to exogenous reasons. And just as we noted earlier [18], extensively drug-resistant strains (XDR-strains) and pandrug-resistant strains (PDR) were detected in 11.1 % and 3.7 % cases accordingly among *K. pneumoniae* isolated from patients treated in the examined cardiac surgery hospital. Moreover, *K. pneumoniae* strains produced beta-lactamases with a wider action spectrum in 92.6 % cases. Presence of HAP agents with polyresistance to antibiotics indicates that hospital clones of microorganisms causing group incidence might occur among them.

Patients with HAP had various background somatic pathologies as well; respiratory diseases, diseases of the endocrine and central nervous system were the most frequent

Table 4

Frequency of typical and prenosological hospital acquired pneumonia among patients, sex-dependent distribution

Sex	AV for less than 48 hours			AV for more than 48 hours		
	A number of patients	HAP cases		A number of patients	HAP cases	
		abs.	per 1000		abs.	per 1000
Men	968	69	71.2 [58.9–89.3]	67	29	432.8 [312.2–556.6]
Women	772	22	28.5 [17.9–42.8]	45	21	466.6 [316–621.2]

Table 5

Microorganisms isolated from children and adults with typical and prenosological hospital acquired pneumonia (per 100 examined patients)

Microorganisms	AV for less than 48 hours (n = 91)		AV for more than 48 hours (n = 50)		Total (n = 141)	
	Number of strains	per 100 examined patients	Number of strains	per 100 examined patients	Number of strains	per 100 examined patients
Staphylcoccus aureus	6	6.5 [2.5–13.8]	4	8.0 [2.2–19.2]	10	7.1 [3.3–12.6]
Staphylcoccus epidermidis	4	4.4 [1.2–10.8]	1	2.0 [0.1–10.6]	5	3.5 [1.2–8.1]
Streptococcus pneumoniae	2	2.2 [0.3–7.7]	1	2.0 [0.1–10.6]	3	2.7 [0.4–6.1]
Enterococcus faecalis	2	2.2 [0.3–7.7]	0	0	2	1.4 [0.2–5.0]
Enterococcus faecium	1	1.1 [0.03–7.7]	1	2.0 [0.1–10.6]	2	1.4 [0.2–5.0]
Acinetobacter baumannii	2	2.2 [0.3–7.7]	1	2.0 [0.1–10.6]	3	2.7 [0.4–6.1]
Pseudomonas aeruginosa	4	4.4 [1.2–10.8]	6	12.0 [4.5–24.1]	10	7.1 [3.5–12.6]
Escherichia coli	4	4.4 [1.2–10.8]	3	6.0 [1.3–16.5]	7	4.9 [2.0–9.9]
Klebsiella pneumoniae	11	12.1 [6.2–20.6]	14	28.0 [16.2–42.4]	25	17.7 [11.8–25.1]
Morganella morganii	2	2.2 [0.3–7.7]	0	0	2	1.4 [0.2–5.0]
Candida	15	16.5 [9.5–25.2]	7	14.0 [5.8–26.7]	22	15.6 [10.4–22.6]

Table 6

Frequency of background somatic pathology among patients with typical and prenosological hospital acquired pneumonia (%)

Background somatic pathology	A number of patients with background somatic pathology among those who spent some time on AV					
	Less than 48 hours (n = 91)		More than 48 hours (n = 50)		Total (n = 141)	
	abs.	%	abs.	%	abs.	%
Respiratory diseases (COPD, bronchitis, bronchial asthma, emphysema, lung infarction)	24	26.4 [17.7–36.6]	22	44.0 [29.9–58.7]	46	32.6 [24.9–41.0]
Endocrine diseases (diabetes mellitus, obesity)	30	32.9 [23.5–43.6]	9	18.0 [8.6–31.4]	39	27.6 [20.5–35.8]
Acute cerebrovascular accident (stroke)	7	7.7 [3.2–15.2]	5	10.0 [3.3–21.8]	12	8.5 [4.5–14.4]
Diseases of the genitourinary system (urolithiasis, pyelonephritis, kidney masses, prostate adenoma)	2	2.2 [0.3–7.7]	2	4.0 [0.5–13.7]	4	2.8 [0.8–7.1]
Perinatal CNS lesions	6	6.6 [2.5–13.8]	16	32.0 [19.5–46.7]	22	15.6 [10.4–22.6]
Previous heart surgery due to congenital heart diseases	3	3.3 [0.7–9.3]	2	4.0 [0.5–13.7]	5	3.5 [1.2–8.1]

(in 32.6, 27.6 and 15.6 % cases accordingly). Others were not so frequent, including acute disorders of cerebral circulation, previous heart surgery due to congenital heart diseases and diseases of the genitourinary system (in 8.5, 3.5 and 2.8 % cases accordingly) (Table 6). We established a statistically significant growth in frequency of respiratory diseases and diseases of the central nervous system among patients with HAP who spent more than 48 hours on AV than among those who spent less than 48 hours on it: from 26.4 to 44.0 and from 6.6 to 32.0 % accordingly ($\chi^2 = 4.6$ and 15.8, $p = 0.03$ and 0.001 accordingly). *RR* amounted to 1.7 (1.0–2.6) and 4.8 (2.0–11.6) accordingly. Therefore, respiratory diseases and diseases of the central nervous system are risk factors of HAP; this might be due to non-specific resistance being suppressed in such patients [13, 19].

We have established earlier that children and adults who are treated in cardiac surgery hospitals after all kinds of open and closed heart surgery may face the risk of hospital acquired purulent septic infections (PSIs) [20, 21]. HAP is more frequent but there can also be infections in areas of surgical interventions, infections of the urinary tracts, and sepsis. We have shown that hospital acquired PSIs, HAP in particular, primarily occur among children and adults being treated in cardiac surgery hospitals not due to an operation itself but due to consequent treatment in ICUs with its duration depending on a type of a performed operation. We have also revealed that the more time patients spend in ICUs, the longer such an epidemiologically significant procedure as AV lasts. The present work highlights a special role played by AV as a risk factor of developing HAP in patients treated in a cardiac surgery hospital.

Conclusions:

1. Most cases of hospital acquired pneumonia occur in patients who are treated in an intensive care unit at a cardiac surgery hospital after heart surgery. We have proven the role played by artificial ventilation as a leading risk factor that can cause pneumonia.

2. We have detected higher incidence rates among children treated in an intensive care unit at a cardiac surgery hospital than among adults. *Klebsiella pneumoniae* is established to be the primary infectious agent that causes pneumonia.

3. Background respiratory diseases and diseases of the central nervous systems are endogenous risk factors of developing hospital acquired pneumonia among patients treated in an intensive care unit at a cardiac surgery hospital.

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