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ORIGINAL PAPER

UPPER RESPIRATORY TRACT INFECTIONS AND INFLUENZA-LIKE ILLNESSES AMONG HEALTHCARE WORKERS: ARE SEROLOGICAL TESTS USEFUL IN MONITORING INFLUENZA AND INFLUENZA-LIKE ILLNESS?

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Abstract

Background: Healthcare workers (HCWs) are at high risk for exposure to upper respiratory tract infections (URTIs) and influenza-like illnesses (ILIs). The present study aimed to surveil URTIs and ILIs and their impact among the Department of Pediatric Infectious Diseases in Wroclaw employees and evaluate their humoral response to influenza. **Material and Methods:** Thirty-six HCWs participated in the first season and 32 HCWs in the second season during years of the study. The authors carried out a URTI/ILI surveillance, and all HCWs were asked to complete a weekly report during 2 influenza seasons: 2016/2017 (S1) and 2017/2018 (S2). In S1 both IgG and IgM antibodies against influenza A and B were assessed. The HCWs with symptoms of ILI were encouraged to undergo PCR tests for influenza. **Results:** No significant differences in reporting URTI were found among vaccinated and non-vaccinated HCWs and HCWs and the control group. Depending on the year 5.5–17.2% of HCWs were treated with antibiotics because of URTI. In the study 58.7% of participants in S1 and 66.7% in S2 decide to work despite the URTI symptoms. There was no statistical relationship between the concentration of anti-influenza IgG and the number of URTIs and ILIs reported. Only vaccinated were willing to undergo voluntary influenza testing. **Conclusions:** The URTI and ILI occur commonly in HCWs, and HCWs contract URTIs as often as the control group. Despite their medical education, HCWs work with the symptoms of infection and overuse antibiotics to treat the URTI. Serology testing is not able to follow the infection's dynamics or identify the people immune to the influenza-like illness. The diagnostic value of IgM antibodies in acute influenza infection is negligible. Vaccinated HCWs are more focused on their health and are more willing to undergo influenza tests. Med Pr. 2022;73(6):441–7

Key words: IgM antibodies, vaccination, humoral response, influenza, healthcare workers, influenza-like illness

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INTRODUCTION

Healthcare workers (HCWs) caring for patients are at high risk for exposure to influenza or other upper respiratory tract infections (URTIs) and influenza-like illnesses (ILIs) by direct and indirect contact, droplets, and aerosols, and by aerosol-generating procedures [1]. However, the vaccination rate among HCWs in Poland is low, despite being officially recommended [2].

The present study aimed to surveil URTIs and ILIs and their impact on work among the Department of Pediatric Infectious Diseases in Wrocław, Poland employees and evaluate their humoral response to influenza in 2 consecutive epidemic seasons.

MATERIAL AND METHODS

The study participated employees of the Department of Pediatric Infectious Diseases in Wrocław, Poland (doctors, nurses, lab technicians, and office workers). It is the only hospital ward in the voivodship that admits children with infectious diseases, including those with severe course and complications. A large percentage are patients with respiratory diseases, including

influenza and RSV. During 2 years in the study participated 36 HCWs in the first season (age Me = 38 years, 94% females) and 32 HCWs in the second season (age Me = 40 years, 94% females). The authors carried out a URTI/ILI surveillance for this study, and all HCWs were asked to complete a weekly report during 2 influenza seasons: 2016/2017 (S1) and 2017/2018 (S2). Participants responded via a specially created mobile application. The surveillance system was in operation for 17 weeks in S1 (from December 12, 2016 to April 10, 2017) and for 13 weeks in S2 (from January 29, 2017 to April 30, 2018) – the observation period depended on the epidemic situation in the region. Real-time information about ILI symptoms, vaccination history, days off from work, doctor's visits, medications, hospitalizations, missed social and sports events, and loss of financial benefits were collected. In S1 611 reports were evaluated, and 97.2% of participants completed all surveys. In the following year, the authors obtained 356 reports, and 71.9% of participants completed all surveys. The ILI was defined as fever with cough, and URTI as the presence of at least 1 of the symptoms: cough, sore throat, hoarseness, headache, or chest pain. Epidemiological data has been compared with influenza reports from the National Institute of Public Health.

Voluntary vaccination against influenza was provided free of charge by the employer. In S1 trivalent influenza vaccine and in S2 quadrivalent vaccine was used. The general vaccination coverage rate was 66.7% in S1 and 72% in S2.

In S1 both IgG and IgM antibodies against influenza A and B were assessed using commercial EIA tests in pre-season and post-season serum samples. Samples were considered positive if the IgG antibody concentration was calculated as ≥22 relative units (RU) per ml and IgM as ≥1.1 RU/ml Sera were not diluted. The HCWs with symptoms of ILI were encouraged to undergo a test for influenza (a nasopharyngeal swabs to perform PCR assay).

These results were compared with those in the control group, primarily students. In S1 203 participants (age Me = 22.9 years, 65% females), took part in the study, and in S2 – 100 participants (age Me = 24 years, 69% females). They were asked to complete the same questionnaire as HCWs. In S1 3437 reports were evaluated (97% of participants completed all surveys) and 1110 in S2 (80% of participants completed all surveys). The general vaccination rate against influenza was 54.2% in S1 and 64% in the following year. The same serological tests in S1 were performed in the control group as in HCWs. The PCR assay was not performed in this group.

Statistical analysis was performed using the Statistica v. 13.0 program. MS Excel 2010 was used to collect data and support statistical analyzes. The value of 0.05 ($\alpha = 0.05$) was adopted as the critical significance level (α) for statistical tests.

RESULTS

In S1 29 HCWs (80.6%) reported at least 1 episode of URTI, 18 of them were vaccinated (75% of the vaccinated group), and 11 were not (92% of the unvaccinated group). The HCWs reported all episodes of URTI during the whole season for an average of 2.7 weeks, unvaccinated HCWs for 2 weeks, and vaccinated for 3.05 weeks. In S2 18 HCWs (56%) reported URTI – 12 of them were immunized (52% of the vaccinated group), and 6 were not (67% of the unvaccinated group). Both vaccinated and unvaccinated HCWs declared the same mean duration of URTI symptoms during the whole season – 1.8 weeks.

The most frequently reported symptoms were sore throat (61% in S1 and 44% in the following year), headache (58% and 39%), cough (53% and 39%), hoarseness (33% in both seasons), fever (19% and 22%) and chest pain (8% and 11%). The percentage of HCWs with URTI seeking health advice was 30.5% in S1 and 22.2% in S2. Five participants (17.2%) were treated with antibiotics because of URTI symptoms in S1 and 1 person (5.5%) in S2. Most sick HCWs preferred self-medication: 82.7% in S1 and 77.7% in the following year. No participant was hospitalized during both seasons. HCWs with URTI: 12 (41.3%) in S1 and 6 (33.3%) took some days off from work in the following year. Among HCWs with ILI (fever, cough, and other symptoms), days off took 5 out of 7 persons in S1 and 1 out of 4 in S2. The others worked despite the disease symptoms. Four (11%) participants in S1 and 2 (6.25%) in the following year lost financial benefits because of the illness. Twelve HCWs (33%) in S1 could not participate in a social event, and 5 (15.6%) in S2.

Control group

In S1 175 control group participants (86.2%) reported at least 1 episode of URTI, 97 of them were vaccinated (86,6 % of the vaccinated group), and 78 were not (85.7% of the unvaccinated group). They reported all episodes of ILI during the whole season for an average of 2.65 weeks. In S2 63 participants (63%) reported URTI. Forty of them were vaccinated

Table 1. Impact of upper respiratory tract infection (URTI) on healthcare workers (HCWs) and control group during influenza season 2016/2017 (S1) and 2017/2018 (S2) in Wrocław, Poland

Variable	Influenza season			
	2016/2017		2017/2018	
	HCWs (N = 36)	control (N = 203)	HCWs (N = 32)	control (N = 100)
Vaccination coverage rate [%]	66.7	54.2	72.0	64.0
At least 1 episode of URTI [%]	80.6	86.2	56.3	63.0
Duration of UTRI symptoms	2.7 weeks	2.7 weeks	1.8 weeks	2.3 weeks
Medical appointment [%]	31.0	78.0	22.2	19.0
Antibiotic treatment [%]	17.2	7.5	5.5	15.9
Loss of financial benefits [%]	11.0	19.0	6.25	17.4
Loss of social event [%]	33.0	47.0	15.6	20.6

(62.5% of the vaccinated group), and 23 were not (63.8 % of the unvaccinated group). The average time of reported ILI was 2.3 weeks.

In the control group most frequently reported symptoms were sore throat (75.6% in S1 and 73% in the following year), headache (65.1% and 63.5%), cough (75.6% and 58.7%), hoarseness (47% and 57%), fever (32.5% and 20.6%) and chest pain (15.7% and 17.5%). In S1 31 (78%) persons with URTI symptoms had a medical appointment, and 12 in S2 (19%). Thirteen participants (7.5%) were treated with antibiotics because of ILI symptoms in S1 and 10 (15.9%) in S2. No one was hospitalized in both seasons. Students with URTI symptoms reported learning difficulties because of the illness – 70.9% in S1 and 63.5% in S2. Moreover 19% out of sick students in season 2016/2017 and 17.4% next year lost financial benefits because of the illness. In 2016/2017 season 47% of them could not participate in a social events, and 20.6% in 2017/2018 season.

No significant differences in reporting URTI were found among vaccinated and non-vaccinated HCWs and HCWs and the control group. The impact on both groups is presented in Table 1.

Humoral response

Before S1 specific IgG against influenza A virus have been detected in 32 HCWs (88.8%) and specific IgG against influenza B virus in all of them. The geometric mean antibody concentration (GMC) against influenza A was 78.9 RU/ml and against influenza B 97.6 RU/ml. In the control group, specific IgG against influenza A virus have been detected in 145 persons (75.1%), and specific IgG against influenza B virus in 159 (82.4%). The geometric mean antibody concentration in control with positive IgG against influenza A was 58.7 RU/ml and against influenza B 70.2 RU/ml.

At the end of S1 among HCWs, IgG against influenza A was positive in 34 (94.4%) and against influenza B in 35 (97.2%). The geometric mean antibody concentration was 78.4 RU/ml (influenza A) and 104.1 RU/ml (influenza B). In the control group after influenza season, positive IgG against influenza A was detected in 167 persons (86.5%) and against influenza B in 180 (93.3%). The geometric mean antibody concentration against influenza A was 71.1 RU/ml and against influenza B 97.9 RU/ml. Among HCWs, influenza A seroconversion was observed in the sera of 2 persons (5.6%) – 1 vaccinated and 1 not. In the control group seroconversion rate for influenza A was 15% (29 persons, including 20 vaccinated) and for influenza B, 12.4% (24 persons, including 22 vaccinated).

Before S1 positive IgM against influenza A and B were detected in 27.8% and 25% of HCWs and 9.8% and 9.3% of the control group, respectively. After influenza season IgM were positive in 44.4% (influenza A) and 36.1% (influenza B) of HCWs and in 20.2% (influenza A) and 18.1% (influenza B) of controls.

There was no statistical relationship between the concentration of anti-influenza IgG antibodies before the epidemic season, and the number of URTIs and ILIs reported in both groups. A significant increase in seropositive IgM persons was observed in the control group. The results of serological testing in the HCWs and the control group are presented in Tables 2 and 3.

Data from the National Institute of Hygiene in Warsaw (the influenza monitoring center for Poland) shows that in S1 99% of influenza infections

Table 2. Seropositivity and specific IgG antibodies concentration among healthcare workers (HCWs) and control group before and after influenza season 2016/2017 (S1) in Wrocław, Poland

Variable	Participants (N = 239)			
	HCWs (N = 36)		control (N = 203)	
	before S1	after S1	before S1	after S1
Influenza A				
IgG				
positive [n (%)]	32 (88.8)	34 (94.4)	145 (75.1)	167 (86.5)
range [RU/ml]	28.9–161.4	23.9–161.1	22–160.2	22.8–176.3
antibody concentration (GMC) [RU/ml] (M)	78.9	78.6	58.7	71.1
seroconversion [n (%)]	2 (5.6)		29 (15)	
Influenza B				
IgG				
positive [n (%)]	36 (100)	35 (97.2)	159 (82.4)	180 (93.3)
range [RU/ml]	31.8–171.7	27.2–191	22.9–201.2	27.9–203.5
antibody concentration (GMC) [RU/ml] (M)	97.6	104.1	70.2	98.0
seroconversion [n (%)]	0		24 (12.4)	

Table 3. Specific IgM influenza A and B among healthcare workers (HCWs) and control group before and after influenza season 2016/2017 (S1) in Wrocław, Poland

IgM seropositivity	Participants (N = 239)			
	HCWs (N = 36)		control group (N = 203)	
	influenza A	influenza B	influenza A	influenza B
Before S1 [n (%)]				
positive	10 (27.8)	9 (25.0)	19 (9.8)	18 (9.3)
negative	26 (72.2)	27 (75.0)	174 (90.2)	175 (90.7)
After S1 [n (%)]				
positive	16 (44.4)	13 (36.1)	39 (20.2)	35 (18.1)
negative	20 (55.6)	23 (63.9)	154 (79.8)	158 (81.9)

in Poland were caused by influenza A virus and 1% by influenza B virus. In Europe influenza A (H3N2) virus dominated, and vaccination showed moderate effectiveness (38%). In Lower Silesia (province with Wrocław capital city), according to the same Institute number of influenza cases peaked at the turn of January and February. Among studied HCWs, URTI was reported predominately in the second half of January and the last week of February. The majority of cases in the control group were recorded throughout January (without a noticeable peak). In the following season, 29.2% of infections in Poland were caused by the influenza A virus and 70.7% by influenza B. In Europe 36% were type A, 64% were type B, and influenza vaccine effectiveness was 25 to 52% against any influenza. In Lower Silesia influenza cases peaked in late February and early March. The percentage of surveyed HCWs with URTI symptoms peaked in the last week of February and in the control group at the turn of February and March.

The HCWs with symptoms of ILI could decide if they want to undergo a test for influenza – a nasopharyngeal swab to perform PCR assay. In S1 5 swabs were obtained, and all were positive for influenza A;

in the following year 3 swabs were collected, and all were negative. Only vaccinated were willing to undergo a test. No test was performed on unvaccinated employees despite incentives.

DISCUSSION

Most studies about influenza, influenza-like illness, and URTI burden focused on economic aspects, hospitalization rates, length of stay, complications, and mortality among high-risk groups (e.g., elderly people, immunosuppressed, pregnant women). Only a few are focused on losses in private life and consequences for individuals.

The URTI was common in study cohort, resulting in a significant impact on the health, private and professional life of HCWs. Surprisingly, no statistical differences were found in reporting URTI in the control group. A similar effect on daily life and responsibilities was also observed. These findings are like those of Kuster et al. [3] from Canada (for influenza only). They showed that contact with persons with acute respiratory illness, rather than the workplace, was associated with influenza infection.

Generally, 5–17.2% of HCWs and 7.5–15.9% of students were treated with antibiotics because of URTI symptoms. In other studies frequent use of antibiotics among persons with ILI is also reported. In a prospective study from Israel and the Netherlands [4] antibiotic overuse rate for viral infection was 83% in adult patients. This fact is worrying because URTIs are overwhelmingly caused by viruses, and overprescription of antibiotics can cause increasing antimicrobial resistance and side effects in patients [5]. The high percentage of HCWs who took antibiotics because of URTI is worrying because of their medical and educational background.

According to Centers for Disease Control and Prevention (CDC) [6] HCWs with fever and other ILI symptoms should be excluded from work until at least 24 h after they no longer have a fever. Unfebrile HCWs with URTI are allowed to continue working but should wear facemasks. In this study 58.7% of participants in S1 and 66.7% in S2 decided to work despite the symptoms, although some were feverish. In another study [7] 41.4–76.6% of HCWs with ILI cared for patients while ill.

A few studies showed the effect of influenza vaccination on reducing ILI incidence, e.g., in the elderly [8] or HCWs in Saudi Arabia [9]. Reductions in absenteeism from work have also been reported for vaccinated HCWs [10]. However, in the review by Ng and Lai [11], the 967 HCWs group showed that vaccination reduced ILI symptoms by only 0.12 days. Vaccination has not been shown to affect the incidence of ILI significantly. The results of following study are consistent with these observations – no evidence can be found of influenza vaccinations significantly reducing the number of ILI episodes among vaccinated HCWs or vaccinated control group participants.

In the study performed in Germany, seroprevalences of influenza A and influenza B increase gradually during childhood – nearly all children >9 years old had antibodies against influenza A, and in the group >13 years old, 80% had antibodies against influenza B. Furthermore, antibody prevalence against influenza A decreased with age in young adults, and the mean antibody concentration was higher than in older adults. The prevalence of antibodies against influenza B increases with age in adults, and the concentrations of antibodies is similar in different age groups [12]. This study shows that HCWs have higher GMC IgG against influenza A and B than young adults. This could stem from the fact that HCWs are exposed to influenza many times in every influenza season and most of them get vaccinated every year.

It is assumed that a serum HI titer of ≥40 indicates a 50% reduction in susceptibility [13]. Determination of HI titer is a gold standard in influenza serological diagnostics. However, it is technically challenging and performed only in specialized laboratories. For this reason, the author shave chosen to use the more straightforward method – ELISA. Reuman et al. [14] showed that serum ELISA-IgG titers predicted influenza severity. No correlation was found between the number of ILI or URTI episodes reported and the level of pre-season IgG anti-influenza antibodies. However, no severe course of influenza was observed in study cohort.

Positive IgM is considered generally an indicator of acute infection and should disappear within a few weeks or months. The appearance of IgM is also a typical effect of vaccinations. The expected observation, the increase in the percentage of people with positive influenza IgM after the season, was only observed in the control group. Moreover, the authors show that 25–27.8% of HCWs (people often exposed to influenza) and 9.3–9.8% of control group have positive IgM even before the influenza season. Anjorin and Nwammadu [15] showed that in Lagos (Nigeria), 56.6% of the examined pregnant women were IgM seropositive for influenza A. A study performed on mice has shown that influenza-virus-specific IgM antibodies persist for the lifetimes of mice (>600 days). This applies to mice vaccinated and infected with influenza [16]. Results of

this study indicate that influenza IgM also does not disappear quickly and stays positive for at least 1 influenza season in humans. It makes the diagnostic value of IgM antibodies in acute infection low. Other authors also find IgM antibodies ineffective in diagnosing acute influenza virus infection [17]. On the other hand, high IgM antibody titer correlates with lower mortality in severe influenza. It may be due to IgM role in preventing uncontrolled inflammatory response [18].

It is significant that only vaccinated HCWs wanted to undergo a test for influenza. Unvaccinated employees were reluctant to admit to the ILI symptoms. Possible that this was due to shame that they did not get vaccinated. Another explanation is that the vaccinated HCWs and students are more focused on their health and expect sustantial vaccination effects. As far as it is known, no studies were conducted on the emotions, possible shame, and guilt of HCWs who did not get vaccinated and developed an infection.

CONCLUSIONS

The medical profession seems not to be a risk factor for URTIs – HCWs contract infections as often as the control group. The URTI and ILI occur commonly in HCWs, resulting in a significant impact on their health, and private and professional life. Despite their medical background, HCWs works with the symptoms of infection and overuse antibiotics to treat the URTI.

Although changes in antibody concentrations are observed during the epidemiological season, serology testing is not able to follow the infection's dynamics or identify the people immune to the influenza-like illness. The diagnostic value of IgM antibodies in acute infection is negligible.

Vaccinated HCWs are more focused on their health, are more willing to undergo influenza tests, and expect positive vaccination effects. Unvaccinated employees are reluctant to acknowledge to the ILI symptoms.

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