Identification of risk groups for influenza. Percentage of total influenza positive patients with chronic co-morbidity in 2018 was comparable with previous seasons except 2015-2016 season when influenza A(H1N1)pdm09 dominated. CVD, COPD, asthma and diabetes were the most often.

Phylogenetic analysis and antigenic cartography of influenza viruses from the patients included in GIHSN study. A slow antigenic drift of influenza A(H1N1)pdm09 viruses with the accumulation of point mutations in the HA gene was observed. All sequenced viruses (except 1 Saint-Petersburg and 1 Ekaterinburg) belonging to one cluster with one or more substitutions in antigenic sites (C2, 3'flap) 2015-15k sequences. Some viruses contain S183P substitution in H1N1 which increases recognition of host cell receptors and possibly changes viral fitness or immune escape. A(H1N1)pdm09 viruses showed rather high rate of mutations in internal genes PB2, PB1, PA, M and NS.

According to the HA gene phylogenetic analysis influenza A(H1N2) viruses were represented by 3 genetic subgroups: 3Ca (26%), 3Cb (59%) and 3Cc (15%). All sequenced viruses had S245N in NA (+CHO with S247N substitution). NGS sequencing revealed deletion in segment 2 of some 3Ca1 viruses resulting in 11 as truncated PB1-F2 protein, the PB1-F2 truncated viruses clustered together on phylogenetic trees for all segments of genome. According to ToFuGiSAD database 11 as PB1-F2 truncation is unique for A(H1N2) viruses, but all influenza A(H1N1)pdm09 viruses have truncated PB1-F2. Singleton inter-subline influenza A(H1N2) reassortant from Ekaterinburg was found - HA: 3Ca2a, other genes - 3Ca-3.

Influenza B viruses (except two) belonged to Yamagata lineage. Phylogenetic analysis of HA gene showed that influenza B viruses isolated in St. Petersburg belonged to the genetic subgroups 3 (B/Phuket/2373/2013-like). Two viruses of Yamagata lineage belonged to clade 1A (B/Brisbane/90/2008-like) without del 162-163. The results of antigenic cartography of influenza A(H1N1)pdm09, A(H3N2) & B viruses correlated with phylogenetic data.

The results of GIHSN study in Saint Petersburg and Ekaterinburg (Russia) in 2017-2018 season

Methods

SARI patients of all age groups were selected by the GIHSN criteria of inclusion/exclusion in study. All procedures were performed according to GIHSN standardized protocol, Version 6, 10 October 2016. Core questionnaires for patients less than 5 years and for patients 5 years or more were applied across all hospital sites. Investigation was conducted in accordance with the principles of GCP. The study was approved by the Local Ethics Committee. Nasopharyngeal swabs collected in UTM (Copan) were tested by RT-PCR using "Ampliclass" kits (Interlabservice, Russia) for influenza A/B and as a result for subtyping of H1N1pdm09 and H3N2 viruses; Influenza B viruses belonging to Yamagata or Victoria lineage was specified using CDCAP (USA) primers & probes. RSV, MPV, PIV, CoV, HRFV, Adv and Bov were recognized by "Ampliclass ARV screen" kits. Virus isolation, genetic and antigenic analysis was performed for the matched of the vaccine and circulated in Russia influenza strains.

Results

Relative burden of influenza viruses compared to other ARI agents

Determination of age specific dominating epidemiological agents of SARI by results of detection of influenza and other respiratory viruses, Influenza A(H1N1)pdm09, A(H3N2) and B/Yamagata viruses co-circulated in 2017-2018 season. The burden of influenza viruses was higher in adult patients compared to pediatric patients (40.2% and 26.3%, respectively); The ARI agents prevailed in aged (42.1% against 11.6%). RSV was the dominating causative agent of admission in pediatric patients (22.6%) reaching 31.1% in influenza A(H3N2) virus co-circulation. A.RS (17.1%) and AdV (10.1%) were the most common agents among 0-2 years. The dominating agent (36.1%) was RSV. Influenza viruses caused 13.3% of investigated cases.

The burden of influenza and other respiratory viruses by age groups

RV was the reason for hospitalization main of young children aged 0-2 yrs (p<0.002) in contrast to influenza viruses which were detected more often in older age groups (mostly in socially active adult patients aged 18-64 years). RSV and MPV affected more pediatric patients.

Monitoring of influenza and other respiratory viruses activity in 2017-2018

IVE against admission by age groups and virus subtypes. Trivalent inactivated subunit influenza vaccine (TV) "Solvirex" paid from the Federal Budget was used mainly for population immunization in Russia in 2017. Other vaccines available in the country: "Vaccinir," "Fluvax." "Influvax" were paid by patients themselves. A total 58.4 min doses were used for population immunization in Russia, including 2.6 min doses in St. Petersburg (for 48.7% of population). In GIHSN study of 1683 enrollees with complete data, 116 patients were positive for influenza A(H1N1)pdm09, 253 for influenza A(H3N2), 326 for influenza B/Yamagata. The overall IVE was 9%, adjusted IVE - 7%. IVE offered little protection against influenza A(H3N2) and B components (as a result of mismatches vaccine strains and circulated H3N2 and B viruses) but was effective against influenza A(H1N1)pdm09 virus (IVE was 77%).

Key aspects:

The last epidemic caused by co-circulation of A/H1N1pdm09, A/H3N2 and B/Yamagata viruses was characterized by late start, moderate intensity and shorter duration compared to previous one;

2. RSV was dominating agent of SARI among young patients. It circulated actively during each epidemic period along with influenza viruses;

3. A/H1N1pdm09 and B/Yamagata Influenza viruses mismatched the vaccine strains by results of genetic and antigenic analysis in difference from A(H1N1)pdm09 virus, that determined the greatest effectiveness of vaccine against the last virus (77%).

Challenges: Further expansion of geographic of GIHSN study in the country is important to obtain accurate indicators of influenza and IARI impact and to evaluate influenza vaccine effectiveness. Full genome analysis of viruses using NGS is important for the recognition of pathogenicity determinants of influenza viruses.

Acknowledgements: We would like to thank Ciordie El Guerreche-Sebain, Victor Basaga Moreno, Javier Diaz Domingo, Maria Mostet and all GIHSN and Open Health Co. staff involved in all the doctors participating in the study for their dedicated work. We thank the Foundation for Influenza Epidemiology for catalytic financial support of St. Petersburg site.