Resurgence of Pandemic Influenza in Kashmir, North India 2014-2015: Absence of K166Q, D225N and T200A mutations in severe influenza.

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INTRODUCTION

- Following the initial outbreak of A/H1N1pdm09 , periodic resurgences of the virus, with variable morbidity and mortality, have been reported from various parts of India including the temperate Kashmir region of northern India with a demonstrable northern hemispherical seasonality compared to the southern hemispherical seasonality in rest of the country with more tropical geography.
- An outbreak of A/H1N1 with high morbidity and mortality was reported in the summer of 2014 and a study based on genbank data reported mutations as the possible cause.
- Two MIT scientists attributed the higher virulence of the A/H1N1pdm09 to K166Q, D225N and T200A mutations in HA region of the sequences deposited in the Genbank databases.
- We herewith report on an outbreak of A/H1N1pdm09 in 2014-15 that resulted in high morbidity and mortality as also to check mutations that were attributed to higher virulence.

METHODS

- Patients presenting with acute respiratory illness suggestive of Influenza like illness or Severe acute respiratory infection to a tertiary care hospital in Kashmir from October 2014 to April 2015 were recruited.
- After clinical data recording, combined throat and nasal swabs were collected in viral transport medium and tested by real-time RT-PCR for influenza viruses using the CDC protocol.
- All influenza A positive samples were further subtyped using primers and probes for A/H1N1pdm09 and A/H3. Influenza B samples were further subtyped into B/Yamagata and B/Victoria lineages.
- Virus isolation, haemaggglutination inhibition testing, sequencing and phylogenetic was carried out using standard assay procedures.
- All patients received symptomatic therapy and influenza positive patients were administered oseltamivir.

RESULTS

- The 1780 recruited patients (845 male; with age 1 month to 90 years (median) presented with respiratory symptoms of varying severity, 540 (30%) required hospitalization.
- 533 tested positive for influenza [Influenza A=517 (A/H1N1pdm09=437, A/H3N2=78); Influenza B=16 (B/Yamgata=15)].
- About 13% (n=240) had been vaccinated against influenza, having received the NH 2015-16 vaccine, 27 (11.3%) of these influenza positive ILI/SARI compared to 506 (32.9%, p<0.0001) of the unvaccinated patients.

RESULTS contd…

- HA sequencing depicted that 2015 isolates belonged to Clade 6B.1 with clade specific S84N, S162N & I216T signature mutations.
- 13 patients died due to multiorgan failure. HA-sequencing did not demonstrate any evidence of K166Q, D225N or T200A mutation, even in those who had a fatal outcome of their infection.
- No H275Y mutation was reported from pandemic H1N1 positives, hence viruses remained susceptible to oseltamivir.

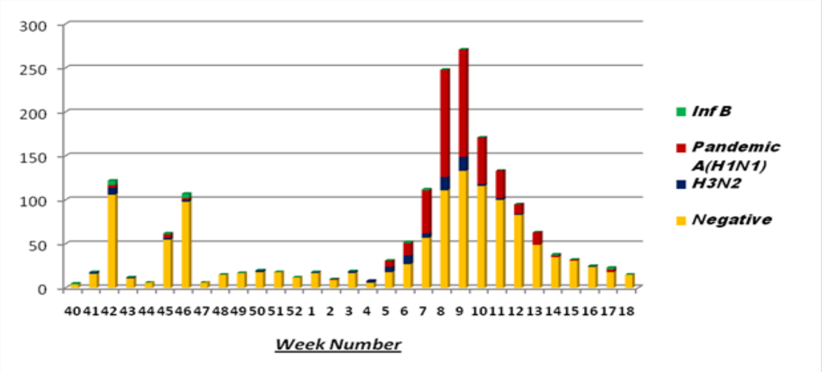

Fig1: Week-wise distribution of Influenza virus in Srinagar

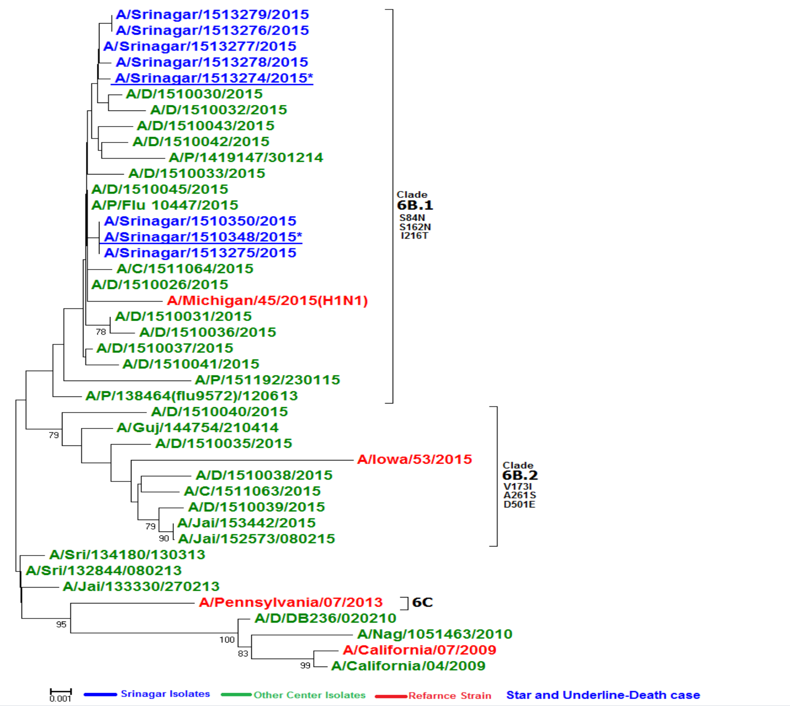

__Figure 2__. HA phylogenetic analysis of 2015 isolates of A(H1N1)pdm09 . The tree consists of 2015 isolates from Pune, Delhi and compared with Srinagar isolates. The astrix and underline isolates are from the fatal severe cases . The 2015-16 vaccine component is shown in red font. Srinagar strains are in blue font. 2015 isolates belong to Clade 7 with clade specific A203T and D97N signature mutations

CONCLUSIONS

- Resurgent outbreak of A/H1N1pdm09 in 2014-15 resulted in high rate of hospitalizations, morbidity and mortality. However, K166Q, D225N and T200A mutations were not found. Periodic resurgences of influenza emphasize adoption of appropriate preventive measures including vaccination.

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