SEROLOGICAL TESTING, INCLUDING IgA ANTIBODY DETECTION, ENHANCES THE DIAGNOSIS OF (SWINE) H1N1 INFLUENZA IN HOSPITALISED PATIENTS.

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Introduction: Diagnostic nucleic acid testing (NAT) on specimens collected from the respiratory tract allows early diagnosis of influenza infection. In the H1N1 2009 (Swine) Influenza pandemic (H1N1 pdm) in Australia in 2009 it soon became apparent that negative NAT results were common in hospitalised patients with clinical illness consistent with H1N1 pdm. In these hospitalised patients delayed presentation, localisation of virus to the lower respiratory tract, and reluctance of clinicians to collect specimens from the lower respiratory tract in patients with severe respiratory disease contributed to these negative results.

Methods: Complement fixation (CF) and H1- swine hemagglutination inhibition (HAI) were used to demonstrate serological evidence of H1N1 pdm I infection CF using Influenza A antigen (Dade Behring) and HAI (A California H1N1 2009) were performed on sera collected from hospitalised patients in South Eastern Sydney with clinical illness consistent with H1N1 pdm between July and November 2009. HAI was also performed on 29 stored sera with elevated influenza A CF titres collected between 2006 and 2008. The results of H1 pdm NAT testing were also available. Serological diagnosis was accepted as a rising titre (at least four fold) or a single elevated (>/= geometric mean (GMT) + 3X s.d. titre of 509 sera collected during this period. Influenza IgA antibody was determined using the Chorus (Dieese) analyser. In addition a set of 29 paired sera collected from patients with suspected influenza in Intensive care units around Australia were also tested by HAI.

Results: The GMT + 3 SD was =64 for CF and =320 for HAI. Serological evidence of H1N1 pdm infection was found in 53 hospitalised patients aged 4-81 years from 850 serum samples were submitted to this laboratory for influenza serology between July and November 2009. In 20 of these 53 patients, specimens for NAT testing had been collected and H1N1 pdm – RNA could only be demonstrated in 4 (20%). The CF failed to demonstrate infection in one 8 year old patient with a significant rising H1N1 pdm HAI antibody titre and positive NAT assay.
All of the *29* paired sera from ICU patients with clinical influenza had significant (greater than four fold) rising HAI titres however only 18 had pandemic (H1N1) 2009 RNA detected by nucleic acid testing. No elevated H1N1 pdm HAI titres were found in 29 stored sera with elevated influenza A CF titres collected between 2006 and 2008. In a set of 21 sera collected from NAT positive patients early (<5 days) in the course of infection15 had diagnostic levels of IgA antibody whereas 12 were positive on HAI and 9 positive on CF.

Conclusions: The study indicates that; i) for the full extent of pandemic influenza cases to be estimated serological testing should be used to augment NAT, ii) laboratories should consider serological testing to establish denominators of infection during pandemics iii) serum should be collected from patients as early as possible in the course of an infection, to allow subsequent comparison of paired sera for serological diagnosis and iv)The traditional complement fixation test will detect most cases of H1N1 pdm v) IgA antibody appears early in the course of H1N1 pdm infection vi) the HAI using A California H1N1 2009 is specific for detecting H1N1 2009 (Swine) Influenza antibody

Notes