Towards control of avian influenza H5N1 virus in Indonesia: Human infection, and the role of live bird markets.

by

Gina Samaan, BPsys (Hons), MAppEpid

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Declaration

I declare that the work contained in this thesis is the result of original research and has not been submitted to any other University or Institution.

The research I conducted and the papers published in this thesis are based on data collected and analysed from a public health surveillance system and three research studies. I was principal researcher in all of the work and played a central role in research design, data collection, analysis and interpretation of findings. For studies pertaining to public health surveillance system data, I facilitated and worked collaboratively with other epidemiologists, statisticians and mathematical modellers to analyze the data and ensure the validity of the findings. For the research studies, I collaborated with laboratory scientists to test collected samples and report microbiological findings. I was solely responsible for overall project management, data management and analysis. I also was responsible for preparation of scientific manuscripts and coordination of co-author input for all papers published as part of this thesis.

The analyses in this thesis are my own work, except where indicated by references or acknowledgements in the text.

Signed: __________________________
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Abstract

Background:
Indonesia has been heavily affected by the emerging avian influenza (AI) H5N1 virus, with continued outbreaks in farmed birds and periodic detection of human cases. The epidemiology of human AI H5N1 infection in Indonesia is poorly understood, and control measures at the animal-human interface such as in live bird markets (LBMs) have had limited impact. This thesis had two aims: (a) to examine the epidemiology of human AI H5N1 infection and, (b) to inform disease control measures in LBMs in Indonesia.

Methods:
For the first aim, public health surveillance data from June 2005 till July 2009 were analyzed to assess exposures and risk factors for infection, case clustering and disease transmission patterns in outbreak households. For the second aim, a cross-sectional study was conducted to assess environmental contamination in LBMs and to identify risk factors and critical control points. A non-experimental field intervention trial was conducted to assess the practical application of implementing interventions in two LBMs.

Results:
Multivariable analyses showed that age and type of exposure to virus impact the risk of H5N1 infection and case clustering. First degree relatives to an index case, especially siblings were at most risk of becoming secondary cases in a household. The overall attack rate in households was 18.3% and the secondary attack rate was 5.5%. Secondary attack rate remained stable with household size. The disease transmission models found that the majority of cases resulted from zoonotic transmission of the virus, and most evidence for human-to-human transmission came from one large outlier cluster of eight cases. The reproduction numbers were below the threshold for sustained transmission. The mean interval between onset of illness between cases in a household was 5.6 days. Direct exposure to sources of virus tripled the odds of infection. Contaminated garden fertiliser was found to be a possible source of human infection.
Widespread environmental contamination with the H5N1-virus was found in 47% (39 of 83) LBMs sampled in the cross-sectional study. Slaughter, workflow zoning and sanitation practices impact the risk of environmental contamination. Five critical control points were identified to help control this contamination. The intervention trial found that control measures could be feasibly implemented using a combination of infrastructure and behaviour change interventions. Use of a participatory approach to translate control measures into practice was well received by stakeholders.

Conclusions:
The epidemiological findings can be used to reduce the risk of zoonotic transmission of the virus, prevent secondary cases and provide baseline comparison for the early detection of changes in virus transmissibility. The LBM studies demonstrated that control measures can be introduced in LBMs in a low resource setting such and that the interventions should reflect resources available, stakeholder needs and critical control points.
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