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A case–control study of occupational risk factors for pancreatic cancer in poultry plant workers: a random forest approach

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ABSTRACT

Background Poultry plant workers are exposed to chemical carcinogens and oncogenic viruses in their work environment. Our objective was to identify jobs and workplaces related to poultries that could increase the pancreatic cancer risk.

Methods We conducted a case–control study within a defined cohort of poultry workers. We used a random forest algorithm to identify features that could increase pancreatic cancer in the poultry plant workers.

Results The mean age of participants was 59.49 years. The majority of the study participants were females (51.30%) and Whites (71.0%). The following workplaces and job tasks had an association with increased pancreatic cancer mortality: working in chicken and turkey plants, working in plants where food products were processed and canned, working in a place where poultry and animals where present, working as a hunter for game animals, working as a veterinarian in places had animals and different poultry birds, working in pet houses and working in places where birds were handled and killed. The accuracy and the area under the curve of the model were 72.3 and 71.50%.

Conclusion Chicken and turkey plant workers could be at risk for pancreatic cancer mortality. We need to confirm the results in future studies.

Keywords cancer, epidemiology, occupational diseases

Introduction

Poultry workers have high exposure to chemical carcinogens and oncogenic viruses in their work environment. The chemical carcinogens they are exposed to are (i) nitrosamines, formed during the curing of poultry [1,2] and (ii) fumes containing polycyclic aromatic hydrocarbons (PAH), benzene and phthalates emitted from the wrapping machines. [3,4] In regards to oncogenic viruses, poultry workers are exposed to viruses that infect and cause cancer in chickens, turkeys and other birds such as Avian leukosis sarcoma viruses (ALSV), reticuloendotheliosis viruses (REV) and Marek's disease virus. [5,6] Some of these viruses can induce cancer in chickens within a week of exposure.[6] These viruses can be transmitted to workers in poultry plants by inhalation, ingestion and skin penetration.[7] Serological tests in this group of workers indicate these viral infections are widely spread. These workers have the highest human exposure to these viruses.[3,8,9] Therefore, poultry plant workers are at high risk for different types of cancers. We reported an excess mortality of lung and liver cancer in these workers in previous two studies.[10,11] Herein, we used a machine learning algorithm—Random Forest—to identify the most important occupational risk factors associated with pancreatic cancer deaths in poultry workers. We conducted a case–control study within a defined cohort of poultry workers—a large-scale case-cohort study—to achieve our goal.

Methods

We obtained the institutional review board (IRB) approval of the University of Arkansas for Medical Sciences.

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The cohort study

For the cohort study, we used the rosters of (i) the United Food and Commercial Workers (UFCW) Meatcutters' Union in Baltimore, Maryland (6 poultry plants), (ii) the UFCW Poultry Union in Marshall, Missouri (6 poultry plants) and (iii) the UFCW Union Pension Fund in Chicago, Illinois, covering 11 poultry plants in six states to define our source population. We identified 30 411 workers who were exposed to poultry through employment in these 23 poultry slaughtering and processing plants located in eight states (Maryland, Delaware, Virginia, Missouri, Arkansas, Louisiana, Maine and Texas). Additionally, 16 405 non-poultry plant workers from ten states (Maryland, West Virginia, Florida, Illinois, Indiana, Massachusetts, New Jersey, Ohio, Pennsylvania and Texas) who were also members of the UFCW Baltimore union or the Chicago Pension Fund, and worked in companies that handled seafood, soft drinks, cheese or oriental food, or manufactured metal containers, etc., were included. [3,8,9,12–14] Thus, the total number of the poultry and non-poultry individuals worked was 46 816 and they were followed up from 1 January 1950 to 31 December 2010.

Case–control study defined within the cohort

In regards to the case–control study defined within the cohort, we identified 56 workers who died from pancreatic cancer (ICD-9 157, and ICD-10 C25) between 1 January 1950 and 31 December 2010. The comparison group included 457 subjects randomly sampled from the cohort. All cases and 15% of the controls were deceased. For deceased cases and controls, we contacted their next-of-kin to collect information on their deceased relatives. We designed a questionnaire to collect data from the subjects if they were alive, or their relatives if they were deceased. We collected information on the study participants' workplace, and their job tasks that could possibly exposed them to viruses or chemical carcinogens. This questionnaire was administered over the phone. The questionnaire included questions on the exposure to the following poultries and animals: chickens, turkeys, ducks, doves, partridges, pheasants, quails, geese, grouses, crows/ravens, cattle, pigs, sheep, goats, horses, bison and game animals, for each poultry, subjects were asked the following questions: (i) If they ever worked in a plant where the poultry was slaughtered; (ii) if they ever worked in a plant where the poultry was not killed, but the plant processed already-killed animal brought in from elsewhere; (iii) if they ever worked in commercial farms handling the poultry; (iv) if they ever worked in a place, or worked for a business, where the eggs of the poultry were handled and (v) if they ever worked in places such as a zoo, pet store, laboratory or other similar places where the animal was handled. Similar but slightly modified tasks in slaughterhouses or processing plants for large animals like cattle and pigs were used. In addition, subjects were asked if they worked in other places or professions, where the previously mentioned viral and chemical exposures could probably occurred such as, the meat and deli departments of supermarkets; restaurants, cafeterias, kitchens; canned food and soup manufacturing plants; places where animals and crops were present; butchers who slaughtered animals, meat cutters (no killing), meat wrappers, veterinarians, meat inspector, gamekeeper, trapper, rancher; work as hunters of game birds (pigeons, pheasants, guinea fowl, etc.) and other game animals (squirrels, rabbits, moose, elk, antelope, deer, etc.), and questions on working in pet stores handling a wide variety of pets (mammals, reptiles, birds and water animals).

Statistical analysis

We explored the role of 22 potential occupational risk factors for cancer in these workers. We used a random forest algorithm to identify the most important occupational risk factors for pancreatic cancer mortality. First, multiple random samples were withdrawn with replacement, from the data—bootstrap. Second, the subset of predictors and observations were randomly selected at each stage to fit a classification tree to each sample. Third, the classifications from trees were combined to obtain improved classification. Finally, voting for classification concluded all these steps. Data were randomly split into two datasets: training (60%) and test datasets (40%). The training dataset was used to tune the number of trees required for the analysis, and the number of splitting variables for the nodes. Because pancreatic cancer mortality is a rare outcome in our study, the algorithm may deviate toward the dominant class (non-pancreatic cancer cases, i.e. the control group; therefore, we oversampled the observations from pancreatic cancer (rarer class) and underdamped the observations of the dominant class (Control). We did that to improve the performance of the classifiers included in the random forest procedure. Recursive feature elimination was used to select the most important variables. We calculated the accuracy and area under the curve (AUC) to evaluate the performance of the model.

Results

Table 1 demonstrates the characteristics of the study population. Figure 1 and Table 2 show the most important risk

Table 1 Characteristics of study population

	Overall (N = 513)
Age	Mean (SD)
	59.49 (10.617)
Sex	N (%)
Male	250 (48.7)
Female	263 (51.3)
Condition	
Control	457 (89.1)
Pancreatic cancer	56 (10.9)
Race	
Whites	364 (71.0)
African Americans	149 (29.0)

factors and their mean decrease in Gini index. We identified eight risk factors for pancreatic cancer out of 22 features. We observed an increase in the cancer mortality risk for those who answered yes to the following questions: (i) Did you work for chicken plants? (ii) Did you work for Turkey plants? (iii) Did you work for a plant where they canned or processed food products such as meat, broth and vegetables? (iv) Did you work in a place where both poultry and animals along with crops where present? (v) Did you work as a hunter for game animals, rabbits, poultry birds, etc.? (vi) Did you work as a veterinarian for large animals and different poultry birds? (vii) Did you ever work in a PET HOUSE or in a pet shop, or in an animal care house or in a place for stray animals where any pet animals, birds, reptiles, fish, etc. were handled? (viii) Did you work in a place where any kind of poultry birds, animals and fish were present, handled or killed for meat? The overall accuracy was 72.30%, and the AUC was 71.50% as shown in Fig. 2.

Discussion

Main finding of this study

The results of this study demonstrated that poultry plant workers, particularly chicken and turkey plant workers, could have an increased risk for pancreatic cancer mortality. We hypothesize that these workers are exposed to poultry oncogenic viruses and chemical carcinogens.[15–19] To replicate the results of our study, we tested the risk of pancreatic cancer mortality in workers not working in poultry plants but could be exposed to similar oncogenic organisms and carcinogenic chemicals that poultry plant workers are exposed to. We observed an increase in pancreatic cancer deaths in people who worked in food canning and soup manufacturing plants, restaurants, or as a cook, etc. This increase could be related to exposure to chemical carcinogens during cooking, or steaming and boiling meat, the results observed in these workers align with those of poultry plant workers. The risk of pancreatic cancer also increased among veterinarians and people who worked with pets. However, we cannot relate the reported increase in risk to animal or bird exposure because those workers—veterinarians and pet house workers—had mixed exposure to both birds and other animals, and pesticides, which complicates interpretation of the results.[20]

What is already known on this topic

Many industrial hygiene assessments indicated that all areas of slaughter and processing plants have high levels of microorganisms, including oncogenic viruses [19,21,22] and workers of these plants have high level of exposure to these organisms. Therefore, several studies reported that workers perform tasks related to chicken—slaughtering and processing—had higher mean antibody levels of two avian oncogenic viruses (ALSV and REV) than workers who never worked in poultry plants.[6,23,24] Workers of poultry plants could be also exposed to PAH and heterocyclic amines (HCA) during poultry meat processing: cooking, frying, steaming boiling, chilling and smoking of meat. PAH and HCA are established causes of cancer including pancreatic cancer in animals or humans. [25,26] Workers involved in smoking and boiling meat in poultry plants have high exposures to PAH and HCA.[18,27]

Limitations of this study

As it is the case with many epidemiological studies, the results should be interpreted in the context of the following limitations. First, this study was case–control study nested within a cohort study and the analysis was exploratory. Therefore, we could not prove causation. Second, we used responses to job workplace as a surrogate for exposure to oncogenic viruses and chemicals because the study's follow-up period was long and all cases were deceased. Thus, the use of a questionnaire to collect information on tasks and areas of work to assess exposure to oncogenic viruses and chemicals was the most convenient and practical method. Third, the study's workplaces are associated with the exposure to many infectious agents – viral, bacteria, fungi, protozoa, and helminths—and chemicals. It was difficult to take into account all these variables in exposure measurement. Fourth, for cases, we collected information on exposure from close relatives; and for controls, we collected information on exposures from the controls if they were alive, and their close relatives if they were dead. Therefore, we expect that recall and interviewer bias might have affected the accuracy of exposures. However,

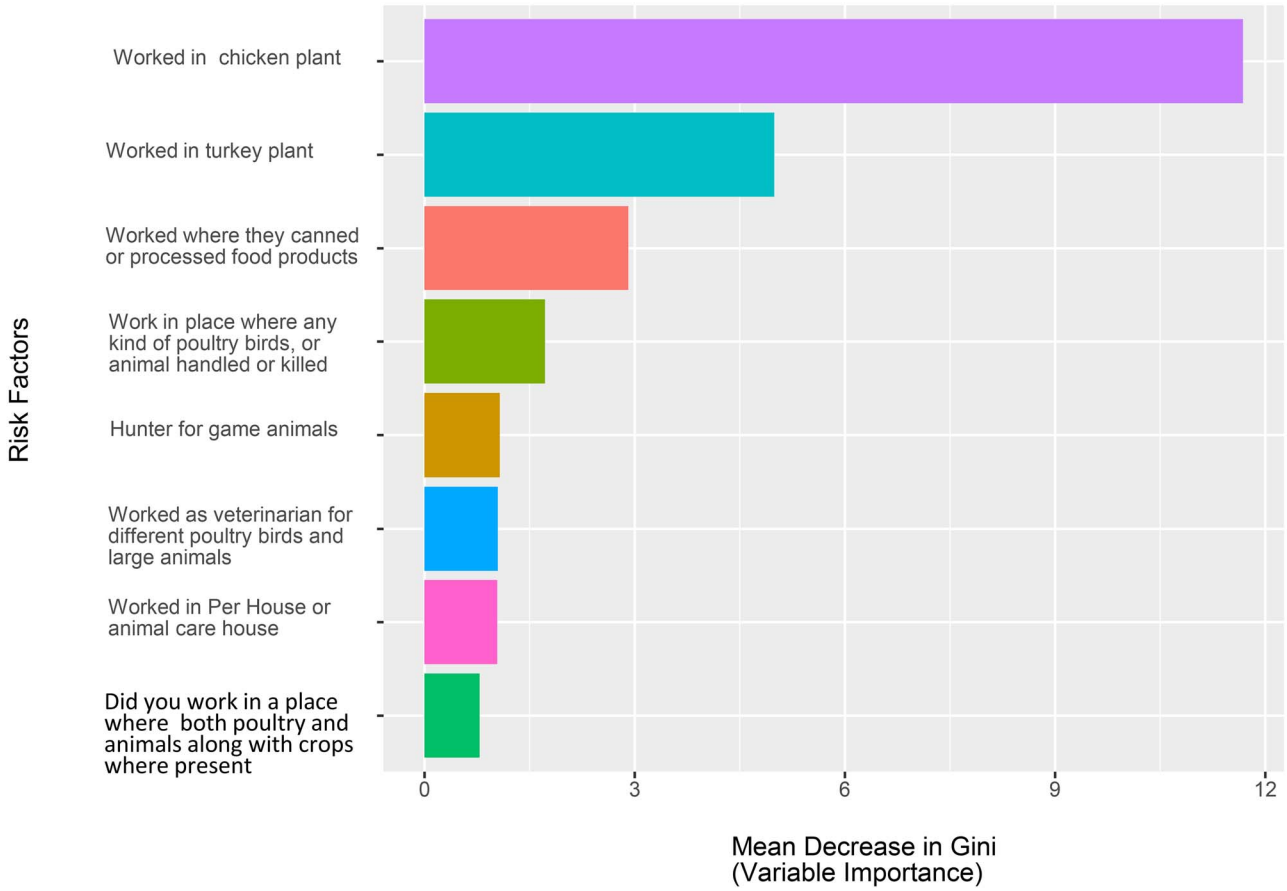

Fig. 1 Rank of risk factors related to pancreatic cancer mortality in the study.

Table 2 The mean decrease in Gini (variable importance) of each feature

Features	*Mean decrease in Gini*
(i) Did you work for chicken plants?	11.68
(ii) Did you work for Turkey plants?	4.99
(iii) Did you work for a plant where they canned or processed food products such as meat, broth, and vegetables?	2.91
(iv) Did you work in a place where both poultry and animals along with crops where present?	1.72
(v) Did you work as a hunter for game animals, rabbits, poultry birds, etc.?	1.08
(vi) Did you work as a veterinarian for large animals and different poultry birds?	1.05
(vii) Did you work in a pet house or in a pet shop, or in an animal care house or in a place for stray animals where any kind of pet animals, birds, reptiles, fish, etc. were handled?	1.04
(viii) Did you work in a place where any kind of poultry birds, animals and fish were present, handled or killed for meat?	0.79

we conducted a validation study to test for the precisions of the responses. We observed a good agreement between the information provided by the living close relatives and living controls: The agreement ranged from 92.5 to 100%. Finally, the accuracy of the model (72.30%) and the AUC (71.50%) were moderate. Had we included non-occupational risk features such as features related to the life style, dietary, personal habits, etc.; the accuracy of classification and identification of workers at risk would be higher. However, we could not do that because of the model over-fitting.

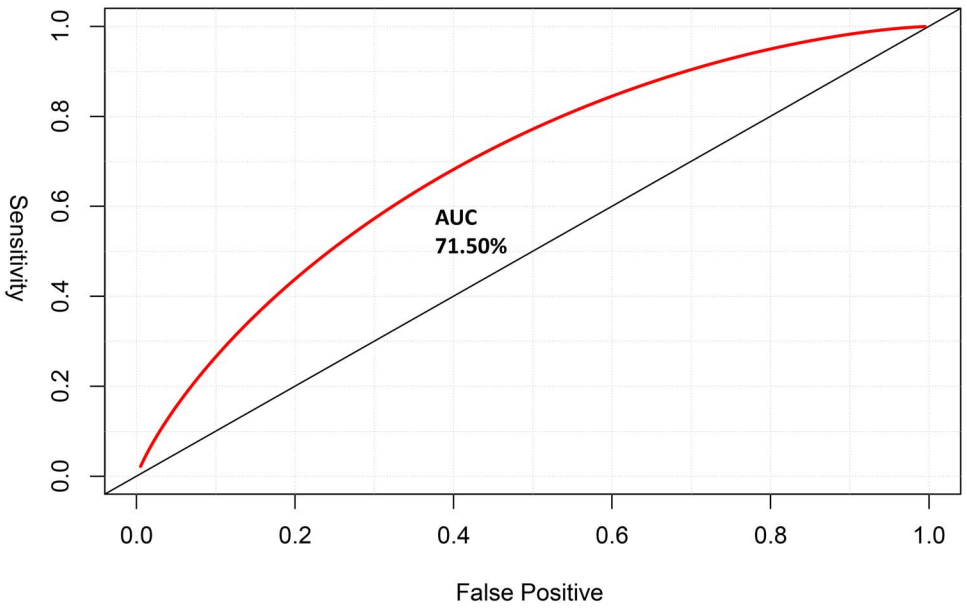

Fig. 2 AUC of the random forest algorithm.

What this study adds

This study is unique because of the following reasons: Frist, to our knowledge, it is the largest and most comprehensive study that explored the risk of pancreatic cancer in the American poultry industry. Second, we used a machine learning algorithms (Random Forest) for the first time to identify risk factors related to pancreatic cancer in these workers; the random forest algorithm allowed us to model complex non-linear and conditional relationships. Third, this study has public health importance because it shines a light on the risk of pancreatic cancer in poultry plant workers. Fourth, the reported increase in pancreatic cancer risk in these workers call for actions and decisions to protect them. We need to educate workers, unions and employers about the potential risks and the protective measures that they need to follow to reduce the risk. Some proposed measures include the design of intervention programs to reduce eczema and injury to the skin through wearing of gloves; improved engineering in ventilation systems to reduce the concentration of airborne infectious agents, or water-borne infectious agents in rinsing water; better enforcement of personal protective measures, personal hygiene, etc., including but not limited to, measures to reduce or eliminate the occurrence of microorganisms (particularly oncogenic viruses) in birds before they arrive at the plants.

In summary, we identified poultry plant workers at risk for pancreatic cancer. The elevated risk could be explained by their high exposure to oncogenic viruses and chemical carcinogens. However, we need to confirm our hypothesized explanation. For example to prove a potential link between carcinogenic viral exposure in poultry plants and cancer, we need to conduct laboratory molecular studies to detect the viral genetic materials integration in DNA of these plants' workers. The isolation of such genetic materials from the poultry plant workers and the results of the epidemiologic evidence can prove that these viruses cause cancer in humans.

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Institution and Ethics approval and informed consent

The protocols and consents—verbal and written—for both the original cohort study and this case-cohort study were reviewed and approved by the Human Subjects Committee (IRB) of the University of Arkansas for Medical Sciences in accordance with the Helsinki Declaration.

Conflict of interest

All authors have no conflict of interests.

Disclaimer

None

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References

1 Sen NP, Miles WF, Donaldson B *et al*. Formation of nitrosamines in a meat curing mixture. *Nature* 1973;**245**:104–5.

2 Sen NP, Donaldson B, Charbonneau C *et al*. Effect of additives on the formation of nitrosamines in meat curing mixtures containing spices and nitrite. *J Agric Food Chem* 1974;**22**:1125–30.

3 Johnson ES, Shorter C, Rider B *et al*. Mortality from cancer and other diseases in poultry slaughtering/processing plants. *Int J Epidemiol* 1997;**26**:1142–50.

4 Vandervort R, Brooks SM. Polyvinyl chloride film thermal decomposition products as an occupational illness: I. Environmental exposures and toxicology. *J Occupat Med* 1977;**19**:188–91.

5 Saif YM, Barnes H.J, Glisson JR *et al*. *Diseases of Poultry*. In: Swayne DES (eds). Ames, IA: Iowa State Press, 2003.

6 Johnson ES. Poultry oncogenic retroviruses and humans. *Cancer Detect Prev* 1994;**18**:9–30.

7 Encyclopedia of Occupational Health and Safety ILO. Geneva: McGraw-Hill, 1998;2–228.

8 Johnson ES, Zhou Y, Lillian Yau C *et al*. Mortality from malignant diseases-update of the Baltimore union poultry cohort. *Cancer Causes Control* 2010;**21**:215–21.

9 Johnson ES, Zhou Y, Yau CL *et al*. Update of cancer and non-cancer mortality in the Missouri poultry cohort. *Am J Ind Med* 2011;**54**:49–54.

10 Faramawi MF, Johnson ES. A case-cohort study to investigate the excess of liver cancer observed in workers in poultry slaughtering & processing plants. *Nutr Cancer* 2019;**71**:1118–31.

11 Johnson ES, Faramawi M, Chedjieu IP *et al*. Excess lung cancer occurrence in poultry plants. Occupational risk factors: findings for oncogenic viruses exposure and other occupational exposures. *Environ Res* 2018;**167**:393–410.

12 Johnson ES. Cancer mortality among workers in the meat department of supermarkets. *Occup Environ Med* 1994;**51**:541–7.

13 Johnson ES, Ndetan H. Non-cancer mortality in poultry slaughtering/processing plant workers belonging to a union pension fund. *Environ Int* 2011;**37**:322–7.

14 Johnson ES, Ndetan H, Lo KM. Cancer mortality in poultry slaughtering/processing plant workers belonging to a union pension fund. *Environ Res* 2010;**110**:588–94.

15 Choi KM, Johnson ES. Occupational exposure assessment using antibody levels: exposure to avian leukosis/sarcoma viruses in the poultry industry. *Int J Environ Health Res* 2011;**21**:306–16.

16 Choudat D, Dambrine G, Delemotte B *et al*. Occupational exposure to poultry and prevalence of antibodies against Marek's disease virus and avian leukosis retroviruses. *Occup Environ Med* 1996;**53**:403–10.

17 Hansen AM, Olsen IL, Poulsen OM. Polycyclic aromatic hydrocarbons in air samples of meat smokehouses. *Sci Total Environ* 1992;**126**:17–26.

18 Nordholm L, Espensen IM, Jensen HS *et al*. Polycyclic aromatic hydrocarbons in smokehouses. *Scand J Work Environ Health* 1986;**12**:614–8.

19 You Y, Leahy K, Resnick C *et al*. Exposure to pathogens among workers in a poultry slaughter and processing plant. *Am J Ind Med* 2016;**59**:453–64.

20 Fritschi L. Cancer in veterinarians. *Occup Environ Med* 2000;**57**:289–97.

21 Goksoy EO, Kirkan S, Kok F. Microbiological quality of broiler carcasses during processing in two slaughterhouses in Turkey. *Poult Sci* 2004;**83**:1427–32.

22 Paba E, Chiominto A, Marcelloni AM *et al*. Exposure to airborne culturable microorganisms and endotoxin in two Italian poultry slaughterhouses. *J Occup Environ Hyg* 2014;**11**:469–78.

23 Johnson ES, Nicholson LG, Durack DT. Detection of antibodies to avian leukosis/sarcoma viruses (ALSV) and reticuloendotheliosis viruses (REV) in humans by ELISA. *Cancer Detect Prev* 1995;**19**:394–404.

24 Johnson ES, Overby L, Philpot R. Detection of antibodies to avian leukosis/sarcoma viruses and reticuloendotheliosis viruses in humans by western blot assay. *Cancer Detect Prev* 1995;**19**:472–86.

25 IARC. *International Agency for Research on Cancer. Monographs on the evaluation of carcinogenic risk of Chemicals to humans. Polynuclear aromatic compounds, Part 4, bitumens, coal-tars, and derived products, shale-oils and soots*, Vol. **35**. France: Lyon, 1985.

26 Jakszyn P, Agudo A, Ibanez R *et al*. Development of a food database of nitrosamines, heterocyclic amines, and polycyclic aromatic hydrocarbons. *J Nutr* 2004;**134**:2011–4.

27 Yao Y, Peng ZQ, Shao B *et al*. Effects of frying and boiling on the formation of heterocyclic amines in braised chicken. *Poult Sci* 2013;**92**:3017–25.