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Agricultural practices and age of chronic myeloid leukemia diagnosis in India

Andrew W. Hill[a,*], Melissa J. Perry[b], Paul H. Levine[a,c]

[a] The George Washington University School of Public Health and Health Services, Department of Epidemiology and Biostatistics, 950 New Hampshire Avenue, NW, 7th Floor, Washington, DC, 20052, USA
[b] The George Washington University School of Public Health and Health Services, Department of Epidemiology and Biostatistics, 950 New Hampshire Avenue, NW, 4th Floor, Washington, DC, 20052, USA
[c] The University of Nebraska Medical Center College of Public Health, Department of Epidemiology, 984395 Nebraska Medical Center, Omaha, NE, 68198-4395, USA

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ABSTRACT

Background/objective: Within India, chronic myeloid leukemia (CML) mean age at diagnosis is 38 years. This study investigated agricultural practices and patterns corresponding to regional variations in CML epidemiology in India.
Methods: Multivariable linear regression and a Cox proportional hazards assessment were used to determine associations between age of CML diagnosis and crop-specific regions.
Results: Patients in the agriculture/fishing occupation sector from high rice-production areas developed CML earlier (2.71 years) than those living in areas with lower levels of rice production (p-value = .01).
Conclusions: These data show a geographic relationship between crops grown and mean age of CML diagnosis. Whether crop type is a reflection of differences in specific occupational chemical uses or dietary practices, and how each of these factors relates to CML risk requires investigation at the individual level.

1. Introduction

Chronic myeloid leukemia (CML) is a rare hematological cancer that starts in the blood-forming cells of the bone marrow. Information regarding the epidemiology of CML in low- and middle-income countries is still emerging, but some recent studies have begun to fill this this gap.[1] The Glivec International Patient Assistance Program (GIPAP), established through a partnership between Novartis and The MAX Foundation, provides treatment and monitoring to eligible CML patients in 80 countries worldwide.[2,3] Using GIPAP data, we recently reported considerable variation in CML age at diagnosis in different populations worldwide,[2] and in India, the average CML age at diagnosis is approximately 38 years;[2] for reference, the average CML age of onset in the U.S. is approximately 64 years.[4] The large number of GIPAP patients in India (14,167) allowed a more detailed analysis of different factors and revealed that patients who were self/employed and worked in agriculture/fishing were more likely to be diagnosed at a younger age than patients working in the government.[5] Additionally, within India, CML age at diagnosis varies geographically.[1] Agriculture practices in India differ according to crops, and crops are not evenly geographically distributed (Fig. 1).[6]

Agricultural communities in India have potentially high exposures to pesticides, herbicides, and insecticides.[7–9] Exposures to agricultural chemicals have been linked to health problems. In three studies conducted in the U.S., Blair et al. investigated the association of agricultural practices with leukemia cell types,[10–12] and in two death certificate studies in Nebraska and Wisconsin they identified an elevated risk of leukemia among farmers.[10,11] The third study categorized the counties of Nebraska according to agricultural practice (dairy, corn, etc.) and assessed odds ratios for different leukemia cell types by predominant agricultural practice of the counties.[12] The authors concluded that focus on specific cell types is needed to better evaluate the role of farm practices in the origin of leukemia. Given the earlier age of onset of CML in patients in India employed in agriculture/fishing found previously,[5] this study was undertaken to explore a possible correlation between specific agricultural patterns and regional variations in CML age at diagnosis in India.

2. Materials and Methods

2.1. Population and agricultural data

State area (in km^2) and land use statistics from each state within India were obtained from the online database of the Agriculture Census

* Corresponding author. Present Address: 545 1/2 W. Arlington Place, Apartment 306, Chicago, IL, 60614, USA.
E-mail addresses: andrew.hill@PAREXEL.com (A.W. Hill), mperry@gwu.edu (M.J. Perry), paulhlevine@earthlink.net, Paul.Levine@unmc.med (P.H. Levine).

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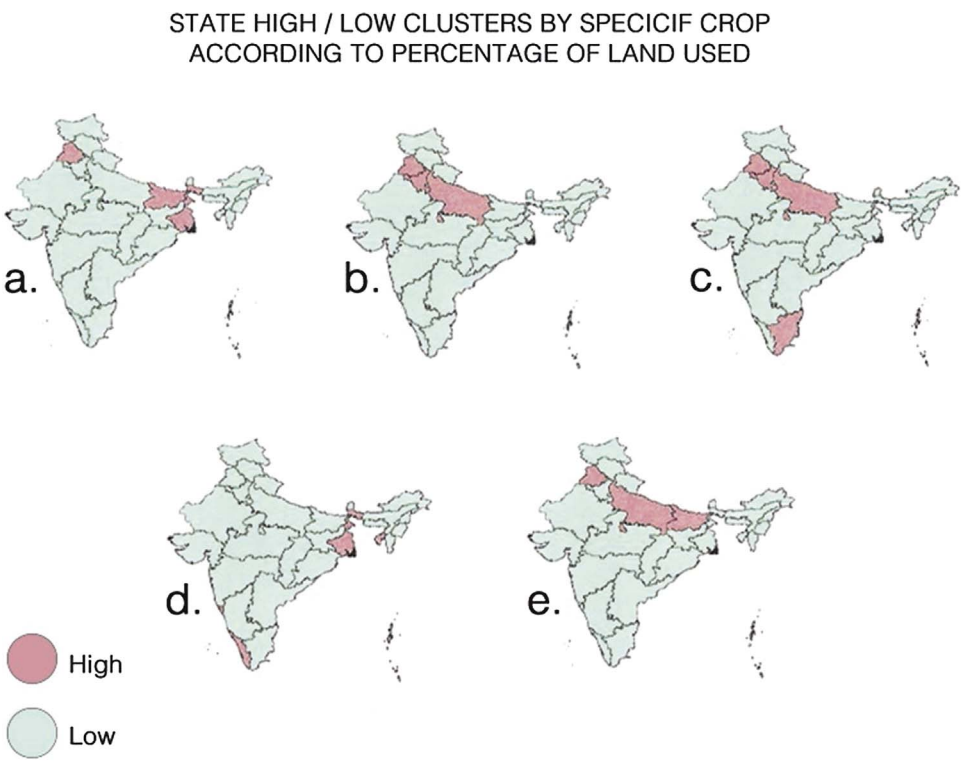

Fig 1. State High/Low Clusters by Specific Crop According to Percentage of Land Used.
*Data from online database of the Agriculture Census in India conducted by the Department of Agriculture and Co-operation.
The top 10% of states per each crop's land use (determined by univariate analysis using the 90% quantile cutoff) was considered to be "high" while the rest of states were considered "low."

a. rice
b. wheat
c. sugarcane
d. fruits & vegetables
e. corn

in India conducted by the Department of Agriculture and Co-operation.[6] The gross cropped area (in hectares) used by each state was then abstracted for specific crops in 2000–2001: wheat, corn, rice, and sugarcane. The dataset did not separate individual fruits and vegetables, but rather combined them into one broad category. The fruits-and-vegetables category included the following: mango, apple, banana, grapes, guava, citrus, pineapple, cauliflower, potato, onion, tomato, cabbage, ginger, and turmeric. The gross cropped area (in hectares) used by each state within India was obtained for the broad category fruits-and-vegetables from the 1999–2000 census data. The gross cropped area in hectares was then converted to km^2. Census data from the years 1999–2000 were selected to best reflect the CML diagnosis date from the GIPAP centers.

The CML patients' age at diagnosis, occupation, and state of residence were obtained from the GIPAP service program of Novartis run by the MAX Foundation.[3] All diagnosis dates for CML patients were before 2009. The occupation category had data for the listed occupation of the patient's head of household (who may or may not have been the patient). This original occupation variable had approximately 25% missing data and had a wide range of occupations listed.

2.2. Endpoints

The primary analysis examined differences in mean age at CML diagnosis for patients residing in high production states versus low production states for the following crops: corn, wheat, rice, sugarcane, and fruits/vegetables. A secondary analysis examined differences in age at CML diagnosis in high production states versus low production states (for all crops examined) in patients with agriculture/fishing occupations versus all other occupations.

2.3. Statistical methods

To determine crop specific land use percentages, each state's total area (in km^2) was used as the denominator, and each state's total gross cropped area per each of the five crops identified earlier was used as the numerator.

States within India were ranked according to land-use percentage based on each of the five chosen crops to assess cutoff points for categorizing states into high or low production. Using univariate analysis, the 90% quantile cutoff point determined high-percentage states. The 90% cutoff point was chosen to better assure that only high-yielding states were considered "high" to draw appropriate conclusions. Thus, the top 10% of states per each crop's land use was considered to be high and the rest were low (Fig. 1).

The mean, standard deviation (SD), and the median were found for CML age at diagnosis for the entirety of India. The distribution of the age of CML diagnosis followed a normal distribution, so the mean (as opposed to median) was then determined for each state within India.

The MAX Foundation dataset combined the occupations for