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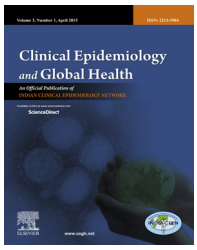

Original Article

Demographic factors related to young age at diagnosis of chronic myeloid leukemia in India

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ABSTRACT

Background/objectives: We have found that chronic myelocytic leukemia (CML) is diagnosed at an earlier age in poorer populations than in more affluent populations. We had used data from the Glivec® Patient Assistance Program (GIPAP) involving 33,985 patients from 94 participating countries and documented the geographic variation in CML age of onset, with low income identified as a major risk factor for early age of onset. As India is the largest cohort within GIPAP, we studied several demographic factors in this population to investigate other possible contributors to early age at onset.

Methods: We analyzed data collected 2002-2008 from 14,167 Indian patients to investigate demographic factors related to age at diagnosis focusing on income and occupation as risk factors.

Results: As in the first study, patients with an earlier age at diagnosis of CML were more likely to be in families with lower annual income. In addition, we found age at diagnosis varied across different occupations; 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. Geographic variation in age at CML diagnosis was also observed, possibly reflecting the influence of environmental and socioeconomic factors on the pathogenesis of CML.

Conclusions: Environmental factors apparently play a major role in determining age of diagnosis of CML. Analytic studies are needed to determine the relative importance of various exposures such as to herbicides/pesticides, dietary habits and other factors related to income to identify specific contributory factors in the pathogenesis of CML.

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Abbreviations: CML, chronic myeloid leukemia; GIPAP, Glivec International Patient Assistance Program.

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1. Introduction

Chronic myeloid leukemia (CML) is a relatively rare disease, less common than the other forms of leukemia. Incidence rates of CML vary globally with the highest rates in Italy, Australia, and the United States, and the lowest rates in Asia.[1] In the United States, it primarily occurs in adulthood with a median age of 64.0.[1,2] CML is characterized by the presence of the Philadelphia chromosome resulting from the fusing of the ABL1 gene on chromosome 9 and the BCR gene on chromosome 22.[3,4] Thus far, only one carcinogen has been well documented for CML, that is exposure to radiation.[5,6] Some studies, however, suggest that other environmental exposures, particularly those relating to agricultural work, are associated with increased leukemia risk, including CML.[7–13]

In a recent study using data from the Glivec® International Patient Assistance Program (GIPAP), which was developed to provide imatinib free of cost to uninsured and underinsured patients in developing countries, we noted significant differences in age of diagnosis and overall survival within and between regions, suggesting important geographically related environmental risk factors for CML, independent of the availability of treatment.[14] As India was the largest contributor of patients to this program, with more than 14,000 CML patients receiving Glivec®, we performed a cross-sectional analysis to explore demographic factors in relation to age of diagnosis in this patient population.

2. Materials and methods

The patients in this study were enrolled in GIPAP, which required that they be diagnosed with CML either by the presence of Philadelphia chromosome (Ph+ CML) or the *BCL/ABL* oncogene, were not insured, and were not able to pay for treatment privately.[15,16] Additional information that was collected on the patients in GIPAP included date of birth, date of diagnosis, date of entry into program, date of start of treatment, sex, geographic location, occupation of the primary family source of income, wage earner's income, and disease stage on admission into the program.

This analysis used the administrative data collected during 2002–2008 on 14,940 patients enrolled in GIPAP in India during this study period. The patients were seen in ten regional centers (see Figs. 1 and 2) that were identified by The Max Foundation as having the best equipped centers with large numbers of hematologic malignancy patients, and the ability to maintain the database needed to monitor each patient. Patients were also recruited from the Tata Memorial Hospital in Mumbai, a national center for cancer patients. For this analysis, we included 14,167 patients after excluding 721 without valid age at CML diagnosis, 9 with missing or a non-Indian residence, and 43 without a molecular CML diagnosis (BCR/ABL+ and/or Ph+). We tabulated categorical age at diagnosis (<20, 20–64, ≥65 years) and evaluated distributions of continuous age at diagnosis separately by sex (male, female), disease phase (blast crisis, accelerated, chronic, remission), annual household income (<$1000, ≥$1000), and occupation (agriculture/fishing, government, self-employed, other). Generalized linear model was used to estimate mean age at diagnosis by each covariate with adjustment for the other. Multiplicative interaction terms between annual household income and other covariates were tested individually in fully adjusted models. Missing covariates were coded as a distinct category, so that patients with such will be retained in the model. We also evaluated distribution of age at diagnosis by annual household income (<$1000, ≥$1000) and by other covariates. All analyses were conducted using SAS v.9.3. All tests were two-sided and the level of statistical significance was set at 0.05. Geographic patterns showing the median income of the population of each state and the mean age of CML diagnosis in each state were developed using geographic information systems (GIS).

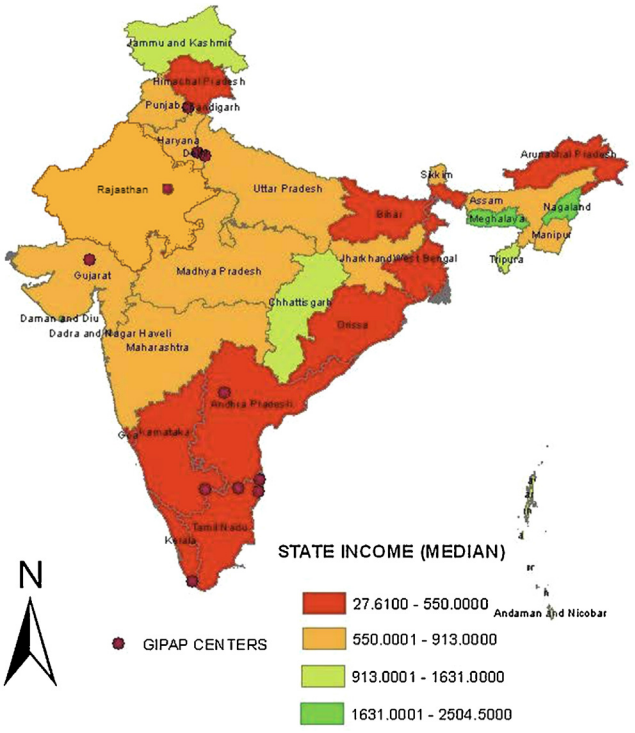

Fig. 1 – Location of GIPAP centers and median income. This figure shows the distribution of GIPAP centers that tend to focus on less affluent and less urban areas than the Indian population-based cancer registries. In general, southeastern India is more affluent than the rest of the country. N.B. These figures are for illustration purposes only and do not represent political boundaries.

3. Results

Patients were diagnosed at a mean age of 38 years (standard deviation [SD] = 14). Table 1 includes patients' characteristics by categorical age at diagnosis. There was a 2:1 predominance of males over females with males being diagnosed at younger ages. The majority (85%) of patients were in the chronic phase. A large portion of patients had annual household income <$1000 (43%) and worked in agriculture/fishing (33%).