Polycythemia Vera Cancer Cluster Investigation

Geographic study of polycythemia vera occurrence in central Pennsylvania (2001–2007)

Study Purpose

The purpose of this study was to look at polycythemia vera (PV) occurrence in a four-county region in central Pennsylvania using methods similar to the previous ATSDR PV investigation in a three-county region in northeastern Pennsylvania.

Background

PV is part of a group of diseases called myeloproliferative neoplasms (MPN). MPNs are a group of blood cancers in which the bone marrow makes too many blood cells. In 2005, several groups of researchers identified a mutation, *JAK2V617F*, present in approximately 97% of PV patients. In 2008, the World Health Organization (WHO) included *JAK2V617F* mutation testing as part of the major criteria for diagnosing PV.

In 2005, using state cancer registry records, Pennsylvania Department of Health (PADOH) found a significantly higher incidence of PV in Luzerne and Schuylkill counties compared to the rest of Pennsylvania. In 2006, PADOH asked ATSDR to help study PV patterns among residents in an area of northeast Pennsylvania. In the original investigation, ATSDR reviewed medical records, conducted genetic testing for the *JAK2V617F* mutation, and confirmed the presence of a cluster of PV at the center of Carbon, Luzerne, and Schuylkill counties in northeast Pennsylvania. Additionally, ATSDR found that more than 50% of PV cases reported to the cancer registry were not PV or there was not enough information to confirm a diagnosis of PV. Underreporting to the cancer registry also occurred; 15 of 33 confirmed cases were not reported.

What Was Studied

In the current study, ATSDR asked PADOH to find out how complete and accurate PV case reporting was to the Pennsylvania Cancer Registry (PCR) from four central Pennsylvania counties (Bedford, Blair, Cambria, and Somerset) for the years 2001–2007. PADOH awarded a subcontract to the University of Pittsburgh's Department of Epidemiology, which conducted the study. The main goals of the study were to:

- better understand and compare PV reporting from a different area of Pennsylvania that was similar demographically to the three-county cluster area in northeast PA
- estimate the true incidence of PV
- determine if the identification and use of the *JAK2V617F* mutation as a diagnostic tool affected underreporting and false reporting of PV

Similar to the original ATSDR PV investigation, the University of Pittsburgh used geospatial methods to find areas having increased cases of PV in the four-county area.

Gathering and Analyzing the Data

The researchers defined "evaluable PV" as persons the PCR identified and classified as having physician-diagnosed PV. To be eligible for the study, patients were required to have:

1) received their physician diagnosis between 2001 and2007 and

2) resided in Bedford, Blair, Cambria, or Somerset counties when first diagnosed.

PV patients not reported to the PCR were identified through enhanced case finding, which included identifying patients by visiting local providers of hematologic services and auditing medical records. Patients with evaluable PV were contacted by a follow-up procedure that included PADOH introductory letters, University of Pittsburgh Cancer Institute recruitment letters, telephone contacts, and home visits. All study participants were offered a *JAK2V617F* mutation blood test and their medical records were obtained and reviewed.

Medical records were reviewed by an expert panel to confirm cases of PV; panel members used a series of case diagnostics schemes to confirm cases. With this information, PV underreporting rates and false reporting rates were calculated. Additionally, the researchers determined how the PCR captured confirmed cases of PV. The researchers used statistical analysis to estimate PV rates for the four county area after correction for under and false reporting. Finally, geospatial analysis using SaTScan was performed to identify areas with potential clusters of PV.

Conclusion and Key Results

The researchers found that the rate of PV in the central Pennsylvania counties of Bedford, Blair, Cambria, and Somerset in 2001–2007 was similar to that of PV in the northeast PA three-county cluster area.

- Spatial scans tentatively identified a cluster of PV cases in the small borough of Bellwood in Blair County: five patients, 60 years of age or older at diagnosis. Three of the cases were found through routine case reporting and two through enhanced case finding.
- Using the most stringent PV case definition, the authors found that 48% of the PV cases in the four counties reported to the cancer registry were confirmed. The number of confirmed cases reported increased with less restrictive case definitions.
- Of patients diagnosed with PV between 2001 and 2007, 18% were not reported to the cancer registry. However, the false reporting rate for the current study, using the most stringent case definition, was 58%.
- Underreporting of PV was more frequent during 2005 through2007 than 2001 through2004.

Similar to the original ATSDR PV investigation, underreporting and false reporting of PV occurred in the central Pennsylvania four-county area.

- The current study found that the 2001–2005 average annual incidence of confirmed PV ranged from 1.3 per 100,000 persons to 3.2 per 100,000 persons in the four-county area. This incidence is similar to that calculated using published data from the original ATSDR PV investigation.

The current study included limitations and challenges similar to previous PV investigations.

- PCR case confirmation procedures rely heavily on hospital reporting. However, PV is a chronic condition commonly diagnosed and treated in outpatient settings, which leads to underreporting.

- PV is often difficult to diagnose. For example, PV may be confused with secondary polycythemia, excessive red blood cell production secondary to other medical conditions such as chronic lung disease with chronic hypoxia.
- Reports of the association between the *JAK2617VF* mutation and PV began to appear in medical literature in 2005. The *JAK2V617F* mutation test isn't used everywhere, affecting the accuracy of PV case reporting and possibly resulting in biased temporal or geographic patterns observed in population-based cancer registries.

For More Information

Visit ATSDR's Web page on PV: http://www.atsdr.cdc.gov/sites/polycythemia_vera/index.html.

Call ATSDR's toll-free PV information line – 866-448-0242 – or email Dr. Elizabeth Irvin-Barnwell, ATSDR Division of Toxicology and Human Health Sciences, at jcx0@cdc.gov.

Contact Lora Siegmann Werner, ATSDR Region 3, at 215-814-3141 or by email at lkw9@cdc.gov.