

ORIGINAL RESEARCH

A National Survey of Hemochromatosis Patients

Arch G. Mainous III, PhD, Michele E. Knoll, MA, Charles J. Everett, PhD, Mary M. Hulihan, MPH, Althea M. Grant, PhD, Cheryl Garrison, BS, Gerald Koenig, BA, Cynthia Sayers, BA, and Kelsey W. Allen, MPH

Background: Hereditary hemochromatosis (HH) is a common genetic disease in the United States, but little is known about the diagnosis from the patient's perspective. The purpose of this study was to characterize the circumstances surrounding the diagnosis of HH and assess treatments and health information needs.

Methods: We surveyed US adults aged 18 years and older who were diagnosed with HH after 1996. Response rate was 46%, with a total sample size of 979. Respondents were asked about the use of genetic and clinical markers in their diagnosis, current treatments, and health information needs.

Results: Results were stratified by age, education, and income status. Total of 90.0% of women and 75.5% of men were genetically tested for HH ($P < .01$). Approximately half (52.5%) were diagnosed by a gastroenterologist, hematologist, or other specialty physician and half were diagnosed by a primary care provider. Most of the respondents thought their HH had improved with the initial treatment and most patients were still receiving treatment for HH. Patient interest in learning more about specific hemochromatosis topics was generally high.

Conclusions: Since the introduction of genetic identification of HH, these tests have been used in the diagnosis of the majority of patients. Primary care physicians may need to be more aware HH and strategies for diagnosis. (J Am Board Fam Med 2012;25:432–436.)

Keywords: Health Care Surveys, Hemochromatosis, Hematology

Hereditary hemochromatosis (HH) is one of the most common genetic diseases found in white Americans and can be fatal if not treated.^{1,2} HH is an autosomal recessive disease that results from significant iron overload due to hyperabsorption of iron from the diet.^{1–3} Historically, HH has been clinically diagnosed with biological markers of iron

overload, specifically elevated transferrin saturation and elevated ferritin, and then treated with phlebotomy.^{4,5} Early detection and treatment of blood disorders are consistent with the mission and objectives of Healthy People 2020.⁶

In 1996, the hemochromatosis gene (*HFE*) was identified and 2 HH-associated mutations were identified: *C282Y* and *H63D*.⁷ According to US prevalence studies, approximately 6.6 million Americans are homozygous for the *C282Y* or *H63D* mutations of *HFE* while another 6 million are compound heterozygotes, possessing one each of these mutations.² Compound heterozygotes and *H63D* homozygotes are at minimal risk for HH whereas *C282Y* homozygotes comprise the vast majority of people with HH. It is unclear how great of an impact the identification of the hemochromatosis gene has had on the diagnosis of HH. Thus, the purpose of this study was to investigate the use of genetic testing as well as to assess the health information needs among individuals in the United States diagnosed with HH after 1996.

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From the Department of Family Medicine, Medical University of South Carolina, Charleston (AM, MK, CE, KA); the Division of Blood Disorders, Centers for Disease Control and Prevention, Atlanta, GA (MH, AG, CS); and the Iron Disorders Institute, Taylors, SC (CG, GK).

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Corresponding author: Arch G. Mainous III, PhD, Department of Family Medicine, Medical University of South Carolina, 295 Calhoun St., Charleston, SC 29425 (E-mail: mainouag@muscd.edu).

Methods

We conducted a survey of HH patients, aged 18 years and older residing in the United States, who were diagnosed with HH after 1996. We focused on individuals diagnosed after 1996 so that they had the opportunity to be diagnosed by both genetic and clinical markers.

We worked closely with the Iron Disorders Institute (IDI) to identify a patient population for study. The IDI is a nonprofit patient support and advocacy organization that promotes hemochromatosis education. It is not a tertiary care center and does not provide clinical care. The IDI patient database is the largest and most comprehensive listing of patients with HH in the United States. This survey and study was approved by the Medical University of South Carolina's institutional review board.

Survey Design

We used a mail survey strategy that has been successfully demonstrated to achieve acceptable response rates.⁸ An initial mailing was sent out, inviting individuals from the IDI database to participate. Three follow-up mailings were sent to nonresponders, and phone calls were attempted for the final nonresponders.

Variables

The respondents were asked if they were ever diagnosed with HH by a doctor or health professional. If they answered yes to this query, they were asked, "What type of doctor or health professional gave you the diagnosis of hemochromatosis?" The response options were family medicine/general practice, internal medicine, gastroenterologist, hematologist, and other. We categorized family medicine/general practice and internal medicine as primary care. The respondents were asked if they were ever genetically tested for HH; then, if they answered affirmatively, they were asked if the genetic testing was performed before a diagnosis of iron overload, after a diagnosis or iron overload, or to confirm a diagnosis of HH.

The types of treatment that respondents received at initial diagnosis were assessed. Respondents were asked if they improved with the initial treatments. The respondents also were asked about current treatment regimens. The usefulness of resources and information sources were assessed by

the respondents. Finally, demographic characteristics of age, race/ethnicity, sex, and year of diagnosis were collected.

Analysis

We computed descriptive statistics (means, standard deviations, and proportions) of the variables and examined the distributions of the responses. In addition, we stratified answers to the questions about the usefulness of information resources and motivation to access information by age, education, and income status and used χ^2 analysis to examine differences. We also conducted logistic regressions examining variables related to the receipt of different laboratory tests before diagnosis.

Results

Our response rate was 46% (979 of 2121). A total of 50.3% were men, 98.5% were white, 70.0% were 50 years of age or older, 54.3% had undergraduate or graduate degrees, and 29.5% had a household income of more than \$100,000. Also, of those who responded, 38.5% had been diagnosed since 2007 (within 3 years of the survey). Overall, 82.3% of the participants had been genetically tested for HH. Of the participants who had been genetically tested, 25.6% were tested before the diagnosis of hemochromatosis, 28.8% were tested after the diagnosis, and 45.6% were tested to confirm their clinical signs and symptoms. A total of 90.0% of women and 75.5% of men were genetically tested ($P < .01$).

Complaints of fatigue and complaints of painful joints were the only reported signs and symptoms that showed associations with different diagnostic tests before diagnosis. Relationships between complaints of fatigue and complaints of painful joints with testing for ferritin level, transferrin saturation, and liver biopsy and genetic testing are shown in Table 1. These logistic regressions were adjusted for age at diagnosis, sex, and race/ethnicity (non-Hispanic white vs nonwhite or Hispanic). The odds ratio associated with a ferritin level measurement increased if the respondent had a prior complaint of fatigue or a prior complaint of painful joints. Similarly, the odds ratio of a transferrin saturation measurement increased if the respondent had a prior complaint of fatigue or painful joints. The odds ratio of a liver biopsy increased if the participant had a prior complaint of painful joints but not

Table 1. Adjusted Logistic Regressions* for Laboratory Tests and Procedures

| | | |
|------------------------------|------------------|--|
| Ferritin level | | |
| Complaints of fatigue | | |
| Yes | 3.00 (1.77–5.08) | |
| No | 1.00 (—) | |
| Complaints of painful joints | | |
| Yes | 2.20 (1.30–3.73) | |
| No | 1.00 (—) | |
| Transferrin saturation | | |
| Complaints of fatigue | | |
| Yes | 1.44 (1.10–1.89) | |
| No | 1.00 (—) | |
| Complaints of painful joints | | |
| Yes | 1.46 (1.12–1.92) | |
| No | 1.00 (—) | |
| Liver biopsy | | |
| Complaints of fatigue | | |
| Yes | 1.20 (0.89–1.60) | |
| No | 1.00 (—) | |
| Complaints of painful joints | | |
| Yes | 1.44 (1.08–1.92) | |
| No | 1.00 (—) | |
| Genetic testing | | |
| Complaints of fatigue | | |
| Yes | 1.26 (0.89–1.79) | |
| No | 1.00 (—) | |
| Complaints of painful joints | | |
| Yes | 1.30 (0.92–1.84) | |
| No | 1.00 (—) | |

All values provided as odds ratio (95% confidence interval).
*Adjusted for age, sex, and race/ethnicity.

if they had a prior complaint of fatigue. Neither prior complaints of fatigue nor prior complaints of painful joints were related to whether a participant was genetically tested for hemochromatosis.

In terms of physician diagnosis, about half were diagnosed by a gastroenterologist, hematologist, or other specialty physician (52.5%) versus those who were diagnosed by a primary care provider. The vast majority (94.4%) of the respondents had received treatment for HH. Of those who had been treated, nearly all (96.8%) initially had undergone phlebotomy and few (4.6%) had been treated initially with medication. A total of 75.5% said that the symptoms of hemochromatosis the experiences had improved with the initial treatment. A large majority of patients (85.6%) reported currently receiving treatment for HH.

Table 2 indicates the perception of the usefulness of available information resources and types of information sources. Of the respondents, 60.5% thought the Internet was extremely useful or very useful. However, 31.75% of those who were from the <\$20,000 income stratum responded that they had never used this form of media compared with 8.51% of those who make more than \$100,000 each year who said they had never used the internet ($P < .01$). In contrast, 84.3% to 89.7% of the respondents said they had never used video, patient support groups, or live patient education seminars. This phenomenon of low use of video, patient support groups, and live patient education seminars was seen with little differentiation among participants across age, income, and education strata.

Interest in learning more about specific hemochromatosis topics was generally high (Table 3). A total of 77.0% of the respondents were extremely interested or very interested in learning more about treatment for hemochromatosis. Of all respondents, 84.7% were extremely or very interested in

Table 2. Usefulness of Resources and Information Sources

| | Extremely Useful | Very Useful | Somewhat Useful | Not Useful | Never Used Them |
|--------------------------------------|------------------|-------------|-----------------|------------|-----------------|
| Resources | | | | | |
| Health care providers | 21.0 | 31.9 | 39.7 | 6.6 | 0.8 |
| Community-based groups | 25.0 | 24.5 | 13.7 | 2.0 | 34.8 |
| Internet | 28.3 | 32.2 | 25.9 | 1.3 | 12.4 |
| University/ academic medical centers | 6.0 | 8.3 | 9.4 | 2.6 | 73.7 |
| Information sources | | | | | |
| Print | 18.6 | 34.0 | 31.4 | 1.6 | 14.4 |
| Video | 2.1 | 4.4 | 7.2 | 2.0 | 84.3 |
| Patient support groups | 3.7 | 5.2 | 4.2 | 2.3 | 84.6 |
| Live patient education seminars | 3.2 | 3.7 | 2.1 | 1.3 | 89.7 |

All values provided as %.

Table 3. Interest in Learning More about Specific Hereditary Hemochromatosis Topics

| | Extremely Interested | Very Interested | Somewhat Interested | Not Interested |
|--------------------------------|----------------------|-----------------|---------------------|----------------|
| Signs and symptoms | 38.3 | 27.7 | 23.6 | 10.4 |
| Cause and risk factors | 43.4 | 30.4 | 18.3 | 7.9 |
| Information for family members | 40.7 | 27.4 | 19.7 | 12.2 |
| Diagnosis | 36.3 | 28.0 | 21.9 | 13.8 |
| Treatment | 48.5 | 28.5 | 15.3 | 7.7 |
| Self-care tips | 55.7 | 29.0 | 10.1 | 5.2 |
| Diet | 54.2 | 26.7 | 13.8 | 5.4 |
| Preventing complications | 63.0 | 25.2 | 8.2 | 3.6 |
| Genetics | 45.4 | 26.8 | 20.1 | 7.7 |

All values provided as %.

learning more about self-care tips, 80.9% in learning more about diet, and 88.2% in learning more about preventing complications. Among these respondents, those who made less money seemed to be more interested in learning about the aforementioned topics. Of those who made <\$20,000, 72.41%, 70.11%, and 80.46% were extremely interested in learning more about self-care, diet, and information on preventing complications, respectively. In contrast, of those who made more than \$100,000 each year, 50.19%, 46.77%, and 58.17% were extremely interested in learning more about the same topics, respectively ($P < .01$).

Discussion

A key finding of this large national survey of persons with diagnosed HH is that the majority of them have been genetically tested since the introduction of tests for the *HFE* gene mutations. Of those who were genetically tested, 45.6% were tested to confirm their clinical signs and symptoms. These data show that genetic testing is being used primarily to confirm a clinical diagnosis rather than as a screening tool.

The patients found information about hemochromatosis provided via the Internet, their health care provider, and community-based groups to be useful. This reinforces the need for primary care providers to be kept abreast of and educated on current information about the diagnosis and treatment of hemochromatosis. Primary care providers need to know about the health information needs of the patients to effectively direct those patients who want to learn more about hemochromatosis. As might be expected, patient interest in learning more about specific hemochromatosis topics was

generally high. These data can help organizations and health educators in developing education programs and outreach strategies that will help to meet the needs of the patient community.

Most of the respondents thought their hemochromatosis had improved with initial treatment and most patients were still receiving treatment for HH. These findings are consistent with phlebotomy as the standard of care for hemochromatosis. Patients can and are getting appropriate care for their disease.

There are several limitations of this study that need to be noted. First, the response rate was not as high as desired, which limits the generalizability of the results. Second, the survey is based on self-report, for which there may be some recall bias for individuals who were diagnosed several years earlier. However, key health events in an individual's life tend to have high recall.⁹ Third, the survey was sent to persons in a disease-specific database of one organization and may not be representative of the general US HH population. Fourth, because the majority of participants were from similar demographic backgrounds, it is hard to determine if information resources should be expanded to those in different age, income, or education strata. However, diagnosed hemochromatosis tends to be found among middle-aged whites, thereby naturally decreasing the diversity of the potential sample.

In conclusion, hemochromatosis patients in the United States are being diagnosed in specialty care with genetic tests as confirmation of clinical findings. Once diagnosed, the patients nearly universally report receiving standard therapy. The patients do want more information about treatment and self-care. Improving recognition and appropri-

ate diagnosis in primary care, thereby increasing early detection, and providing more resources for disease management are the appropriate next steps in improving diagnosis and treatment of hemochromatosis.

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