Missed Hypothyroidism Diagnosis Uncovered by Linking Laboratory and Pharmacy Data

Gordon D. Schiff, MD; Seijeoung Kim, PhD; Nela Krosnjar; Mary F. Wisniewski, MSN; Judylin Bult, PharmD; Leon Fogelfeld, MD; Robert A. McNutt, MD

Background: Although diagnostic errors are important, they have received less attention than medication errors. Timely follow-up of abnormal laboratory test results represents a critical aspect of the diagnostic process, and failures at this step are a cause of delayed or missed diagnosis, resulting in suboptimal clinical outcomes and malpractice litigation. We linked laboratory and pharmacy databases to (1) explore the potential for linking laboratory and pharmacy databases to uncover diagnostic errors, and (2) determine the frequency of failed follow-up of elevated levels of thyroid-stimulating hormone (TSH).

Methods: We downloaded TSH test results for 2 consecutive years from a laboratory database and linked this database with a pharmacy database to screen for patients with TSH levels of 20 mU/mL or higher who were not receiving levothyroxine. Patients with elevated TSH levels lacking prescriptions were followed up by telephone and record review.

Results: During the 2-year period, 982 (2.7%) of 36760 unique patients tested for TSH level had elevated TSH levels. Of these patients, 177 (18.0%) had no recorded levothyroxine prescriptions. We attempted to contact 177 patients with high TSH levels who were not taking thyroid medications and reached 123 (69.5%). Of the 123 patients we were able to reach, 12 in 2000 and 11 in 2001 were unaware of their abnormal test results or a diagnosis of hypothyroidism, representing 2.3% of 982 patients with elevated TSH levels. We were unable to reach another 54 patients (5.5% of the total number of patients with elevated TSH levels) by either telephone or mail.

Conclusions: By linking laboratory and pharmacy databases, we uncovered patients who did not undergo follow-up for abnormal TSH results. Conservatively, there was no follow-up for abnormal TSH results in more than 2% of patients, and another 5% of patients were lost to follow-up and possibly unaware of their results. Uncovering patients with missed diagnosis illustrates a potential use of linking laboratory and pharmacy databases to identify vulnerabilities in the care system and improve patient safety.

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We downloaded ASCII files of all inpatient and outpatient TSH results obtained during 2000 and 2001 (recorded in a dedicated clinical data warehouse developed by the Chicago Antimicrobial Resistance Project).13 We also downloaded all outpatient prescriptions for levothyroxine from our pharmacy computer system (TechRx, NDCHealth, Atlanta, Ga) for the same 2-year period. We then linked data from these 2 sources using unique medical record numbers using Access 97 (Microsoft Inc, Redmond, Wash) and SPSS (version 11.0; SPSS Inc, Chicago, Ill). Data sets were created and retrospectively analyzed separately for 2000 and 2001 approximately 6 to 12 months after the conclusion of each calendar year.

While a TSH level of 6.0 mU/mL or higher is the upper limit of normal in our laboratory, we conservatively elected to examine patients with TSH levels of 20 mU/mL whose results unquestionably warrant follow-up.11 For each patient with TSH levels of 20 mU/mL or higher, we then evaluated pharmacy records to determine which patients lacked prescriptions for levothyroxine. To verify that the patient was not receiving levothyroxine currently or in the past 2 years and to check for any other thyroid-related medications prescribed, we also manually reviewed pharmacy computer records for all patients with high TSH levels when our electronic screen failed to find any matching prescriptions in our linked database.

If we found no evidence of use of levothyroxine or other thyroid-related medications from a review of pharmacy computer records, we contacted patients by telephone. We asked whether the patient was aware of the abnormal test results and whether he or she was taking levothyroxine dispensed by another pharmacy. In patients who were not receiving medication or who were not cared for elsewhere, we scheduled another TSH test and arranged appropriate follow-up care.

If we could not reach the patients by telephone, we mailed a letter informing the patient about the abnormal TSH test result and requesting that they contact us. If we could not reach the patients by telephone or letter if additional information was needed to supplement the telephone interviews, we reviewed the outpatient medical records.

The hospital’s institutional review board approved our study protocol, and the hospital’s quality assurance and improvement committee sanctioned the activity as a formal quality improvement project.

Table. Overview of Thyroid-Stimulating Hormone (TSH) Levels and Follow-up Data, by Year

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2000 No. (%)</th>
<th>2001 No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total TSH tests</td>
<td>22 076</td>
<td>24 524</td>
</tr>
<tr>
<td>Unique patients with TSH test results</td>
<td>17 467</td>
<td>19 293</td>
</tr>
<tr>
<td>Test results with TSH levels &gt;20 mU/mL</td>
<td>1334 (6.0)</td>
<td>744 (3.0)</td>
</tr>
<tr>
<td>Unique patients with TSH levels &gt;20 mU/mL</td>
<td>470 (2.7)</td>
<td>512 (2.7)</td>
</tr>
<tr>
<td>Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using levothyroxine</td>
<td>390 (83.0)</td>
<td>415 (81.1)</td>
</tr>
<tr>
<td>Not using levothyroxine</td>
<td>80 (17.0)</td>
<td>97 (18.9)</td>
</tr>
<tr>
<td>Using hyperthyroid medication</td>
<td>17 (3.6)</td>
<td>20 (3.9)</td>
</tr>
<tr>
<td>Who obtained prescription at outside pharmacy</td>
<td>17 (3.6)</td>
<td>34 (6.6)</td>
</tr>
<tr>
<td>Lost to follow-up or died</td>
<td>27 (5.7)</td>
<td>27 (5.3)</td>
</tr>
<tr>
<td>Aware of diagnosis without follow-up</td>
<td>4 (0.9)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>With a missed diagnosis of hypothyroidism</td>
<td>12 (2.6)</td>
<td>11 (2.1)</td>
</tr>
</tbody>
</table>

OVERALL TSH RESULTS AND LEVOTHYROXINE USE

A total of 22 077 TSH tests were performed on 17 467 unique patients in 2000, and 24 524 tests on 19 293 patients in 2001. During 2000, 1334 test results showed a TSH level of 20 mU/mL or higher in 470 unique patients (2.7%). In 2001, 744 test results showed a TSH level of 20 mU/mL or higher in 512 unique patients (2.7%). Of the patients whose TSH level was greater than 20 mU/mL, 80 (17.0%) in 2000 and 97 (18.9%) in 2001 had no recorded prescriptions for levothyroxine (Figure). This matching, performed on unique 7-digit patient identifiers (ie, unit number), appeared adequate in that, on cross-checking, all patient names also matched.

ANTITHYROID DRUGS

When we manually reviewed our pharmacy information system, we discovered that a number of patients who were not receiving levothyroxine were currently taking antithyroid medications such as propylthiouracil. We assumed that these patients had been diagnosed as having hyperthyroidism and that their elevated TSH levels represented excessive treatment rather than unrecognized hypothyroidism. Of the 470 patients in 2000 and 512 patients in 2002 with TSH levels greater than 20 mU/mL, there were 17 (3.6%) in 2000 and 20 (3.9%) in 2001 treated with antithyroid drugs (Table). Of patients with elevated TSH levels who

Figure. Data summary flow sheet. All percentages refer to the 982 unique patients with a TSH level of 20 mU/mL or higher.
were not taking levothyroxine, there were 17 (21.3%) of 80 patients in 2000 and 20 (20.6%) of 97 patients in 2001 with hyperthyroidism due to overtreatment.

OUTSIDE PHARMACY USE

While most of the indigent patients in our public hospital clinic receive their medications from the Cook County Bureau of Health Services pharmacy, some patients obtained their prescriptions at outside pharmacies. When we contacted patients with high TSH levels with no evidence of treatment from our data set, we found that 17 (3.5%) of 470 patients in 2000 and 34 (6.6%) of 512 patients in 2001 obtained levothyroxine from outside pharmacies.

OTHER EXPLANATIONS FOR UNTREATED PATIENTS

In a total of 6 (3 in 2000 and 3 in 2001) patients with high TSH results, the results were from neonatal screening tests, and the results of subsequent follow-up tests were normal. An additional 6 patients (4 in 2000 and 2 in 2001) were aware of their diagnosis of hypothyroidism but, for various reasons, were not being treated.

FAILED FOLLOW-UP OF ABNORMAL TSH LEVELS

Of 123 patients we reached (by telephone or mail), 12 patients in 2000 (2.6% of 470 patients with elevated TSH levels) and 11 patients in 2001 (2.1% of 512 patients with elevated TSH levels) were unaware of their abnormal test results and had never been informed about a diagnosis of hypothyroidism. In addition, we were unable to reach 27 patients in 2000 (5.7% of 470 patients with elevated TSH levels) and 27 patients in 2001 (5.1% of 512 patients with elevated TSH levels) by telephone or mail to determine whether they were aware of the abnormal test results or whether they were receiving treatment. In 12 (52%) of 23 patients who did not receive follow-up and 20 (37%) of 54 patients lost to follow-up, the laboratory tests were conducted during a visit to the emergency department or walk-in clinic. In addition, 4 (17%) of 23 patients who did not receive follow-up and 10 (19%) of 54 patients lost to follow-up, the laboratory tests were conducted during inpatient admission.

COMMENT

By linking laboratory and pharmacy records from a large public hospital clinic system, we were able to identify patients with a missed diagnosis of hypothyroidism. While the subject of follow-up of abnormal laboratory results is often cited as an important quality issue, electronically cross-referencing laboratory test data with pharmacy records is a more novel and potentially useful method to identify such diagnostic error cases. By comparing these data, we were able to identify patients with high TSH levels who were not receiving therapy and follow up with these patients.

Quality improvement expert Berwick emphasized that “every system is perfectly designed to deliver the results it does.” Because our results were virtually identical for both years (Table), for these 2 years, we seem to have a perfectly designed system to overlook a dozen patients each year with a test result suggestive of hypothyroidism and to lose another 27 patients each year to follow-up (for whom we are unable to determine their awareness and treatment of the abnormal thyroid test result). By conservatively choosing a cutoff TSH value of 20 mU/mL, we selected patients unequivocally warranting follow-up. While the test results in some patients with high TSH levels whose diagnosis was missed were normal on retesting, the initial failure to follow up nonetheless represents a failure in the diagnostic process.

The failure to follow up can result from imperfect systems for test result transmission, physician notification, as well as patient-related factors such as missed appointments or other discontinuities in care. Many of the patients with a missed diagnosis had an initial visit in our emergency department or walk-in clinic with no subsequent recorded encounters. Others underwent tests while hospitalized, but the results returned after they were discharged from the hospital. Of the patients contacted who were unaware of their results or diagnosis, none were receiving ongoing primary care from our institution at the time of contact (several were seeing private physicians). Thus, more reliable follow-up processes, both to ensure that abnormal results are addressed and follow-up care is assured, appear to be required, particularly in a public hospital setting where discontinuities in care are not uncommon and resources (patient telephones and staff to contact patients) are limited. This process could also include an enhanced patient role in the follow-up process (ie, increased awareness and ability to access outstanding results).

There are several limitations to our study. In addition to the missed hypothyroid cases, there were 54 patients who could not be reached, and we were unable to determine if they were aware of the abnormal test results or if they received treatment elsewhere. This finding suggests that the number of patients who were unaware of their test results and were not treated (470 [2.7%] in 2000 and 512 [2.7%] in 2001) is a conservative estimate, with actual number perhaps double. Another group of patients received levothyroxine therapy elsewhere and thus were absent from our pharmacy database. The percentage of patients with high TSH levels who filled a prescription at a pharmacy other than Cook County pharmacy increased from 3.6% in 2000 to 6.6% in 2001 (P<.05). This finding is the only significant change between the 2 years and is explained by a policy change in our institution, whereby patients in 2001 with Medicaid drug coverage were encouraged to obtain medication at outside pharmacies. Our study method also did not account for patients with undiagnosed hypothyroidism, for whom clinicians failed to suspect the diagnosis and/or failed to order thyroid tests.

Linking and comparing the laboratory and pharmacy databases uncovered other quality issues, including patients using antithyroid drugs (such as propylthiouracil) who were being overtreated. In addition, while not the focus of our study, we discovered patients who were already diagnosed as having hypothyroidism and who were treated with levothyroxine but who had elevated TSH val-
ues. In these patients, the high TSH levels suggest possible undertreatment, delays in therapy adjustment, or lack of patient adherence to treatment. These other quality issues could also be identified and ameliorated by comparing laboratory and pharmacy databases.\(^\text{10}\)

Whether comparing laboratory and pharmacy databases can be applied to other clinical laboratory–medication pairs to usefully uncover other diagnostic failures requires further study. There is probably a limited set worth exploring, such as undiagnosed diabetes (patients with elevated glucose or hemoglobin A\(_1c\) levels lacking diabetic medications or self-monitoring strips), rhabdomysis or liver disease induced by HMG-CoA reductase inhibitors (statins; patients with elevated creatine kinase or liver enzyme levels using statins), or inappropriate antimicrobial therapy (patients with blood cultures positive for bacteria but lacking antimicrobial therapy warranted for the organisms recovered).\(^\text{12,20,21}\)

Finally, realizing the full potential of comparing laboratory and pharmacy records goes beyond merely identifying gross problems such as laboratory results that have never been followed up.\(^\text{12,16,22-25}\) Electronic tools are needed to fine-tune care. By more closely connecting diagnostic and testing information with therapy, we envision that the role for data linkage will be to overcome problems like the ones we identified, such as delaying or failing to adjust therapy, fine-tuning drug dosing and monitoring, avoiding medications contraindicated by abnormal laboratory results, as well as more quickly recognizing drug-related complications.\(^\text{26-29}\) Such linkages depend on the ability to access data that are highly fragmented in the United States.

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Correspondence: Gordon D. Schiff, MD, Division of General Medicine, Department of Medicine, John H. Stroger, Jr, Hospital of Cook County, 1900 W Polk St, Room 901, Chicago, IL 60612 (gdschiff@aol.com).

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**REFERENCES**


