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Research Article

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Analysis of inappropriate repeated laboratory testing

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Abstract

Objectives: Laboratory services are an important part of the healthcare system. However many requested tests may be considered inappropriate or unnecessary. We evaluated laboratory use in a period of 3 years in terms of the inappropriate test repeats.

Methods: We analyzed inappropriate repeat rate (IRR) of hemoglobin A1c (HbA1c), 25-OH vitamin D [25(OH)D], thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), anti-thyroid peroxidase antibody (anti-TPO), vitamin B12, folate, iron, ferritin and total cholesterol in the light of clinical guidelines.

Results: IRR of 3 year was found to be 10% on average (4.2–15.5%). In TSH, FT3, and FT4 parameters, IRR was between 4.2 and 5.3%, while it was between 12.9 and 15.5% for 25(OH)D, iron, ferritin, and total cholesterol. In all tests (except anti-TPO), IRRs were found to be higher in inpatients for each of the 3 years. Inappropriate repetition of total cholesterol, iron, and ferritin parameters were more frequent in men. Inappropriate repeats were performed in all parameters (except HbA1c) after a result that had been in the reference range.

Conclusions: Examined test repetitions were mostly inappropriate. To reduce the inappropriate laboratory test requests, it is important to analyze the causes and to ensure cooperation between laboratory specialists and clinicians.

Keywords: inappropriate use of the test; medical laboratory; minimum retesting interval; rational laboratory use.

Introduction

Laboratory medicine is one of the high-volume medical activities in healthcare, and the demand for laboratory tests is increasing disproportionately to medical activity [1]. Despite the increasing use of tests, no positive relationship was found between the frequency of laboratory use and patient care quality [2]. Therefore, a significant part of the requested tests is considered inappropriate or unnecessary [3].

The six-R paradigm has been developed to define the concept of appropriateness from the perspective of laboratory medicine; "requesting the right test with the right method, at the right time, to the right patient, to produce the right result at the right (reasonable) cost" has been defined as an appropriate request [4]. It is also important to define inappropriateness. According to a definition, a request made outside the agreed guideline is not appropriate [5]. A common misconception is that inappropriateness can only mean misuse or excessive use of laboratory resources. However, insufficient use is also an important mark of inappropriateness. In a meta-analysis covering the years 1997–2012 conducted by Zhi et al. [6], the inappropriate overuse rate was reported as 20.6%, while the insufficient use rate was 44.8%.

The UK Society of Clinical Biochemistry and Laboratory Medicine made recommendations on the appropriate minimum retesting interval (MRI) in 2013. In clinical biochemistry, therapeutic drug follow-up, hematology, and immunology, they defined optimal MRIs for various tests in a particular clinical situation on evidence-based guidelines [7]. With the MRI, repetition of a test before a specified time can be prevented, depending on the characteristics of the test and the clinical situation in which it is used [8].

In this study, we aimed to evaluate retrospectively and cross-sectionally the laboratory use of our institution in terms of the appropriateness of test repetitions in the 3 years period

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covering 2015–2017, based on objective criteria. For this purpose, tests that have little vital importance even if they are associated with pathological conditions and which have blood levels that are unlikely to change in a short time, with high-volume and high-value were preferred. Accordingly, hemoglobin A1c (HbA1c), 25-hydroxy vitamin D [25(OH)D], thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), antithyroid peroxidase antibody (anti-TPO), vitamin B12, folate, iron, ferritin, and total cholesterol measurements were examined.

Materials and methods

The study was conducted from January 1, 2015, to December 31, 2017, in the clinical laboratory at the Public University Hospital of Bursa Uludag University, Turkey. 25(OH)D, HbA1c, vitamin B12, folate, iron, ferritin, TSH, FT3, FT4, anti-TPO, and total cholesterol test results were evaluated through the laboratory information management system (LIMS). During the 3 year period, there was no change in the methods and devices in which the tests were measured. For each parameter, the data obtained from LIMS includes the patient identifier, registration date, gender, age, test result, the clinical department making request, inpatient/outpatient, and reference interval according to age and/or gender. The patients who had more than one test request during the year were determined through the Microsoft Office Excel 2010 filter function. The intervals between consecutive test requests were determined to identify inappropriate repetitions. Clinical practice guidelines prepared by relevant specialist societies were used to determine the MRI (Table 1). Since there was no recommendation in the guidelines for anti-TPO, expert opinion was consulted. Tests with multiple requests during the year were classified into two groups as "appropriate repeat" and "inappropriate repeat" according to the MRI determined with clinical practice guidelines. Inappropriate repeat rate (IRR) was calculated with formulae: IRR (%) = Number of inappropriate repeat tests/Total number of tests × 100. Inappropriate repeat group was further categorized in subgroups as gender, inpatient/outpatient, and pathological/normal results according to the reference range. Approval for the study was obtained from the local Ethics Committee.

Statistical analysis

Three year data were analyzed. The annual test numbers, annual number of repetitions, and annual inappropriate repetition numbers of each parameter were assessed as a percentage over the years.

Results

In our laboratory, while a total of 6,142,307 and 6,572,389 tests were performed in 2015 and 2016, respectively; this number reached 6,829,202 tests in 2017. The annual number of tests, repeats, and IRRs of the 11 parameters we examined in our study are shown in Table 2.

Table 1: Definition of minimum retesting intervals for analytes.

Tests	Minimum retesting interval	References
Thyroid stimulating hormone	4 weeks	ATA/AACE guidelines clinical practice guidelines for hypothyroidism in adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association [9]
Free triiodothyronine	4 weeks	ATA/AACE guidelines clinical practice guidelines for hypothyroidism in adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association [9]
Free thyroxine	4 weeks	ATA/AACE guidelines clinical practice guidelines for hypothyroidism in adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association [9]
Total cholesterol	6 weeks	AACE guidelines American Association of Clinical Endocrinologists' Guidelines for management of dyslipidemia and prevention of atherosclerosis [10]
25-Hydroxy vitamin D	12 weeks	2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada [11]
Vitamin B12	12 weeks	Guidelines for the diagnosis and treatment of cobalamin and folate disorders [12]
Folate	12 weeks	Guidelines for the diagnosis and treatment of cobalamin and folate disorders [12]
Iron	12 weeks	Guidelines for the diagnosis and treatment of cobalamin and folate disorders [12]
Ferritin	12 weeks	Guidelines for the diagnosis and treatment of cobalamin and folate disorders [12]
Hemoglobin A1c	12 weeks	ADA. Standards of medical care in diabetes-2014 [13]
Anti-thyroid peroxidase antibody	52 weeks	Specialist opinion

For the 11 parameters we examined, the 3 year IRR was 10% on average, ranging from 4.2 to 15.5%. While IRRs for TSH, FT3, and FT4 tests were in the range of 4.2–5.3%, they

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Table 2: Details of inappropriate tests for 11 analytes.

Test	Number of patients	Number of tests	Number of repeated tests	Test repetitions before MRI	Inappropriate repeat rate (%)[a]
Hemoglobin A1c	37,342	55,930	29,900	5,666	10.1
25-Hydroxy vitamin D	105,898	152,467	75,161	22,235	14.6
Vitamin B12	131,109	174,887	74,169	17,410	10.0
Folate	105,463	138,549	56,261	12,774	9.2
Iron	79,567	107,621	44,470	16,731	15.5
Ferritin	82,522	108,600	42,612	13,995	12.9
Total cholesterol	133,296	209,079	114,880	29,938	14.3
Thyroid stimulating hormone	179,766	266,158	136,609	14,101	5.3
Free thyroxine	124,702	188,971	100,338	9,698	5.1
Free triiodo-thyronine	73,890	103,853	49,391	4,410	4.2
Anti-thyroid peroxidase antibody	14,115	15,517	2,609	1,407	9.1

MRI, minimum retesting interval. [a]Inappropriate repeat rate % = Test repetitions before MRI/Total number of tests × 100.

were in the range of 12.9–15.5% for 25(OH)D, iron, ferritin, and total cholesterol tests (Table 2).

When the inpatients and outpatients were considered separately, it was seen that the tests were ordered from outpatients at a rate of up to 94%. However, it was determined that the IRR was higher in inpatients for all tests (except anti-TPO). IRRs of total cholesterol, TSH, FT3, and FT4 tests were 3–4 times higher in inpatients compared to outpatients. As an exception, the IRR of anti-TPO was higher in outpatients (Table 3).

When the parameters were evaluated in terms of gender, it was found that all parameters, especially 25(OH) D and anti-TPO (68.5 and 78.1%, respectively) were more requested in female patients. However, it was determined that male patients were dominant in inappropriate repetition of total cholesterol, iron, and ferritin tests. Female patient dominance was observed only in inappropriate repetitions of anti-TPO. No significant difference was found in terms of gender in the inappropriate repetition of all other parameters (Table 4).

Results of inappropriately repeated tests outside the reference range were defined as "inappropriate repeated pathological result". It (%) was calculated as; Inappropriate repeated pathological result (%) = inappropriately repeated with pathological results / inappropriately repetition number × 100 formula. The most common tests with inappropriate repeated pathological results were HbA1c (84.2%), total cholesterol (55.5%), and ferritin (39.2%). However, folate (9.4%), 25-OH vitamin D (13.7%), FT4 (19.0%), FT3 (26.1%), vitamin B12 (21.9%), and ferritin (39.2%) tests had

Table 3: Frequencies of inappropriate repetition in inpatients and outpatients.

Test	Number of tests	Tests on outpatients, n, %	Test repetitions before MRI on outpatients, n, %	Tests on inpatients, n, %	Test repetitions before MRI on inpatients, n, %
Hemoglobin A1c	55,930	52,492 (93.9)	5,180 (9.9)	3,438 (6.1)	486 (14.1)
25-Hydroxy vitamin D	152,467	144,194 (94.6)	20,465 (14.2)	8,273 (5.4)	1,770 (21.4)
Vitamin B12	174,887	159,292 (91.1)	14,898 (9.4)	15,595 (8.9)	2,512 (16.1)
Folate	138,549	123,277 (89)	10,670 (8.7)	15,272 (11)	2,104 (13.8)
Iron	107,621	94,457 (87.8)	14,203 (15)	13,164(12.2)	2,528 (19.2)
Ferritin	108,600	95,918 (88.3)	11,362 (11.8)	12,682(11.7)	2,633 (20.8)
Total cholesterol	209,079	189,552 (90.7)	23,146 (12.2)	19,527 (9.3)	6,792 (34.8)
Thyroid stimulating hormone	266,158	246,627 (92.7)	10,640 (4.3)	19,531 (7.3)	3,461 (17.7)
Free thyroxine	188,971	171,058 (90.5)	6,955 (4.1)	17,913 (9.5)	2,743 (15.3)
Free triiodo-thyronine	103,853	91,911 (88.5)	3,139 (3.4)	11,942(11.5)	1,271 (10.6)
Anti-thyroid peroxidase antibody	15,517	14,456 (93.2)	1,343 (9.3)	1,061 (6.8)	64 (6)

MRI, minimum retesting interval.

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Table 4: Frequencies of inappropriate repetition in male and female patients.

Test	Number of tests	Tests on female patients, n, %	Test repetitions before MRI on female patients, n, %	Tests on male patients, n, %	Test repetitions before MRI on male patients, n, %
Hemoglobin A1c	55,930	33,081 (59.1)	3,314 (10)	22,849 (40.9)	2,352 (10.3)
25-Hydroxy vitamin D	152,467	104,452 (68.5)	15,088 (14.4)	48,015 (31.5)	7,147 (14.9)
Vitamin B12	174,887	106,578 (60.9)	10,492 (9.8)	68,309 (39.1)	6,918 (10.1)
Folate	138,549	83,018 (59.9)	7,463 (9)	55,531 (40.1)	5,311 (9.6)
Iron	107,621	65,342 (60.7)	9,190 (14.1)	42,279 (39.3)	7,541 (17.8)
Ferritin	108,600	67,787 (62.4)	8,246 (12.2)	40,813 (37.6)	5,749 (14.1)
Total cholesterol	209,079	117,164 (56)	14,179 (12.1)	91,915 (44)	15,759 (17.1)
Thyroid stimulating hormone	266,158	174,405 (65.5)	9,386 (5.4)	91,753 (34.5)	4,715 (5.1)
Free thyroxine	188,971	121,552 (64.3)	6,156 (5.1)	67,419 (35.7)	3,542 (5.3)
Free triiodothyronine	103,853	67,407 (64.9)	2,893 (4.3)	36,446 (35.1)	1,517 (4.2)
Anti-thyroid peroxidase antibody	15,517	12,120 (78.1)	1,153 (9.5)	3,397 (21.9)	254 (7.5)

MRI, minimum retesting interval.

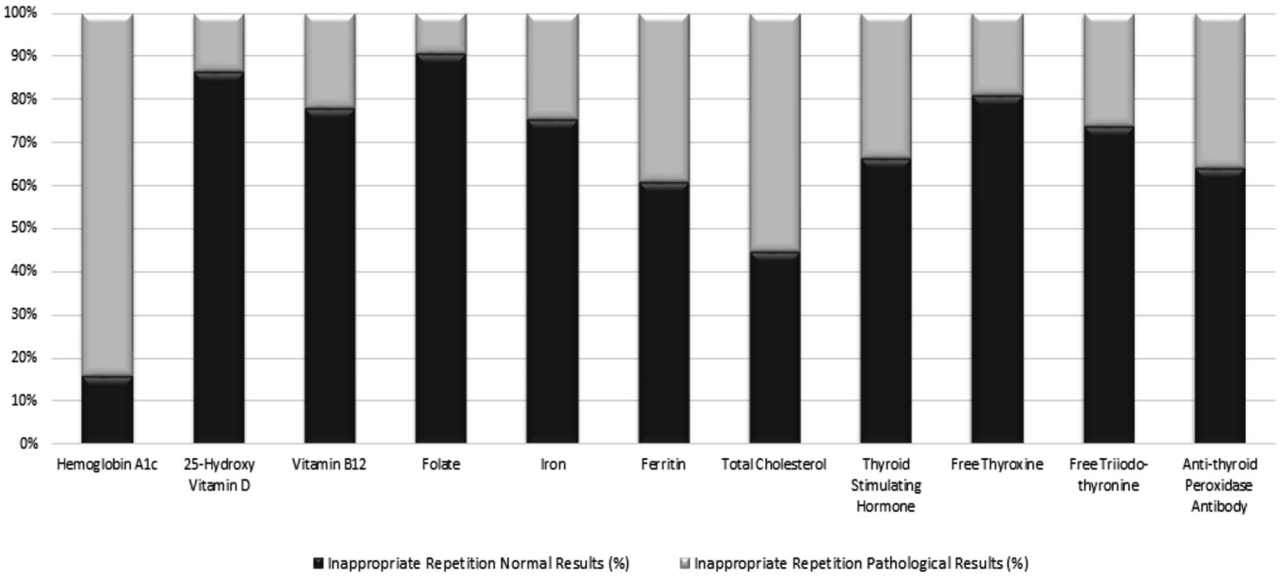

Figure 1: Inappropriate repeated tests based on reference ranges.

the lowest rates in inappropriately repeated pathological results (Figure 1).

When we evaluated IRR according to the requested department, the endocrine clinic was in first place for many tests such as HbA1c (56.1%), 25OH D vitamin (27.0%), TSH (24.5%), FT4 (27.2%), FT3 (26.3%) and was also the most requested clinic for these tests. Pediatric neurology clinic was the department with the highest Vit B12 (18.2%) and folate (23.6%) IRRs, and the highest number of test requests. Iron (33.7%), anti-TPO (27.9%), ferritin (18.2%), and total cholesterol (17.2%) IRRs were the highest in oncology, general surgery, hematology, and oncology departments, respectively.

Discussion

It was found the average IRR was 10% in 3 years. In a study conducted by Chami et al., 9 parameters (HbA1c, vitamin D, vitamin B12, folate, lipid profile, TSH, serum protein electrophoresis, immune fixation electrophoresis, quantitative immunoglobulin determination) were examined and the

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average IRR was found to be 10.6% [14]. In another study carried out by Morgen and Noogler using data from all laboratories in Calgary region of Canada and examining 6 parameters similar to those analyzed in our study, the IRR was reported to be 16.4% [15]. In a study involving the analysis of 6 parameters (total cholesterol, ferritin, vitamin B12, folate, 25-OH vitamin D, 1,25-OH vitamin D) over 3 years in a training and research hospital from Italy, the average IRR was determined as 14.6% [16]. In a meta-analysis covering the years 1997–2012, the rate of inappropriate overuse was found to be 20.6% and insufficient use was 44.8% and inappropriate repetition rate was reported as 7.4% [6]. Our higher rate of IRR compared to this meta-analysis can be explained by the fact that most of the examinations are requested by the assistant or intern physicians whose duty places change frequently since our hospital is a tertiary education and research hospital. In a study conducted by Khromova et al., it was reported that approximately 75% of young doctors do not trust themselves in requesting or interpreting laboratory tests, and they need more training about examinations [17].

In a study conducted by Lanzoni et al., the IRRs for inpatients (minimum 4.6% – maximum 32.9%) were consistent with our study [16]. In a study conducted in Turkey that examined only lipid profile repeats, it was reported that IRRs were performed more frequently in inpatients, in accordance with our findings [18]. Cadamuro et al. suggested that outpatients are at less risk for unnecessary test repetition due to a very short time for test request and blood collection and inpatients are at higher risk for unnecessary test repetition because they are available for blood collection during their stay [19].

The test request was found to be higher in females. On the other hand, it was determined that male patients were dominant in the IRR of total cholesterol, iron and ferritin parameters. Appropriate vitamin D repetitions have been correlated with the female gender in Italy [20]. However, it was found that per capita laboratory test cost is higher for men than women. Men may have required further investigation because they consult a physician in more serious situations than women [21].

IRR of 25(OH)D was found that of 14.6% in a 3 year period. In a study conducted by Morgen and Naugler, IRR was found to be 24.5% for 25(OH)D [15]. However, in their study, inappropriate repetitions of vitamin D results, which were within reference ranges, were examined and the MRI was accepted as 1 year. In another study conducted by Chami et al., the IRR for 25(OH)D was found as 6.88%. In their study, the MRI was taken for 12 weeks, as in our study [14]. According to a study conducted in a training and research hospital like ours in Italy, the IRR for 25(OH)D was found to be 8.2% [16]. The high IRR observed in our study made us think that the test request may also be high due to the high level of vitamin deficiency in our country.

The IRRs were reported as 7.2 and 7.7% for TSH, in some studies [14, 15]. The MRI for TSH was longer (8 weeks) in these studies. In our study, the results of 73.7% of inappropriately repeated thyroid function tests (TSH, FT4, FT3), were within reference ranges. The high IRR in thyroid function tests may be due to endemic iodine deficiency in Turkey. Another test group with a high IRR in the reference range is lipid profile tests. In this study, IRR of lipid profile tests was 14.3% and, 44.5% of these were found to be within reference ranges. In a study conducted in a tertiary hospital in Iran, IRR for lipid profile tests was reported as 30% [22]. This study, in which patients' clinics were examined to decide for inappropriate use of the tests, was different from our study in methodology. IRR for lipid profile in inpatients in a university hospital in Italy was reported to be 2.26% [23]. The reason why the repeat rates differ from our study can be explained by the fact that the relevant study was conducted only on inpatients and the MRI was taken for 50 h. In an investigation conducted at a university hospital in Turkey, where MRI was taken for 4 weeks, IRR was 4.6% for total cholesterol [18]. The IRRs were reported to be approximately 10% for lipid profile or total cholesterol in 3 different studies conducted in Canada and Italy, that used similar MRI (12–13 weeks) [14–16]. Using different patient groups and different MRIs in studies may lead to different detection of inappropriate test rates.

IRRs for vitamin B12, folate, iron, and ferritin, also known as hematinic tests, were determined as 10.0, 9.2, 15.5, and 12.9%; and the rate of inappropriate repeats within the reference ranges for these tests were 78.1, 90.6, 75.3, and 60.8%, respectively. In the studies of Morgen and Naugler, where the MRIs for vitamin B12 and ferritin were determined as 1 year, the IRR with results within reference ranges was 28.4% for vitamin B12, while this rate was 35.8% for ferritin [15]. In a 1 year study for primary care physicians in Spain, including hematinic tests, it was stated that when these tests are used in the light of guidelines, approximately 5 million Euros can be saved annually [24]. In the study conducted by Chami et al., which uses a very similar method to our study, the average IRR was reported as 8.22% for vitamin B12 by using 12 weeks as the MRI. This rate was very close to our rate. In the same study, MRI for folate was determined as 1 year and an IRR of 19.89% was reported [14]. In the study using MRI as 43 weeks for vitamin B12 and folate in Italy, the IRR was reported as 17.5 and 18.2%, respectively. In the same study using a 13 weeks MRI, similar to that accepted in our study for ferritin, it was reported that the IRR was 24.4%. The researchers stated that the IRR value was 13.4% in their

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evaluation by extracting the data of donor and thalassemic outpatients [16]. The high IRR for ferritin observed in this study could be explained by thalassemic or donor outpatients too. It was observed that the test repetitions of the HbA1c tests were mostly composed of pathological results in this study. In a study using the MRI as 12 weeks like us, in patients with abnormal HbA1c value in Canada, 24.8% of IRR was reported [15]. In a study with a similar method to ours, the IRR for HbA1c was reported as 17.7% [14]. In another study conducted in a 2 year period in the USA, it was observed that 6.8% of 130,538 HbA1c tests that were measured below 7% were repeated within 1 month [25]. In a study made in a university hospital in Turkey, it was reported that 35.5% of HbA1c requests were repeated before 90 days [26].

Since HbA1c is a frequently used test in monitoring blood glucose in diabetic patients, it is usual for the majority of inappropriate repetitions to have pathological results. Anemia, vitamin D deficiency, and thyroid diseases are very common in our country. For this reason, tests related to these diseases are very often requested. This may explain that the majority of inappropriate repeat results for folate, 25-OH vitamin D, FT4, FT3, vitamin B12, and ferritin were within the reference range.

By revealing such inappropriate repetitions in different institutions, attention can be drawn to rational and effective laboratory practices. Inappropriate repetitions can be prevented with trainings to be applied to employees and restrictions to be made in the test request.

In conclusion, laboratory tests in health services have great importance in making the correct diagnosis of the patient, monitoring the treatment, and predicting the prognosis. Inappropriate use of laboratory examinations not only harms the patients but also leads to unnecessary additional costs. Different time intervals for retesting in different clinical and treatment situations are recommended in the guidelines. In our study, we used the shortest of these recommended time intervals, considering all patients as the patients who need to be followed most closely according to the guidelines. Although we used the shortest time interval, we found that the test repetitions of the parameters we examined were highly inappropriate. Observation of frequent repetition of parameters, especially with former results within reference ranges, was remarkable. Necessary measures such as analyzing the reasons and collaborating between laboratory professionals and clinicians should be taken to reduce the inappropriateness of laboratory test requests.

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Competing interests: The authors declare that there is no conflict of interest.

Ethical approval: The study was approved by the University of Uludag Ethics Committee (2018–9/13) and was conducted in accordance with the Declaration of Helsinki. This study originates from a thesis

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