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Implementation of the Laboratory and Quality Management in a Turkish Medical Biochemistry Laboratory

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ABSTRACT

Objective: This study aims to show how a biochemistry laboratory in Turkey is managed by national regulations and practices, and thus give the laboratory directors a wider perspective on laboratory and quality management.

Materials and Methods: The pre-analytical, analytical, and post-analytical processes of our laboratory were evaluated according to the national regulations in Turkey by using the data of the patients who applied to our hospital, and the internal and external quality control results of the tests in 2020. Nucleus software was used as the laboratory and hospital information system (LIS/HIS) for data collection, and the Microsoft Excel program was used to analyze the data.

Results: In our biochemistry laboratory, the physical conditions and safety of the laboratory, the recording and storage of electronic data and, the execution of the total testing process (TTP) are by the Medical Laboratories Regulation (Date: 09.10.2013 Number: 28790) and the other national regulations. The evaluation results for 2020 were as follows: Pre-analytical, analytical, and post-analytical error rates were <1%. Total allowable errors (TEa) of 15 biochemical tests were under Turkey TEa limits. Critical values notification rates were >50% and quality indicator rates were <5% for every three months. Our average turnaround times of test groups were within our determined target times.

Conclusion: Our biochemistry laboratory successfully carried out the TTP in 2020. To give the most accurate and cost-effective test results to the patients timely, a lab

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director should manage the laboratory according to national and/or international regulations using medical and mathematical skills.

Keywords: Total testing process, Pre-analytical phase, Quality indicators.

1. INTRODUCTION

A medical biochemistry laboratory is a medical discipline in which clinical laboratory science and technology are used for patient care (Medical Laborotary, Wikipedia). The main goal of the medical biochemistry lab is to provide patients the most accurate and cost-effective results at the right time (WHO, 2011). For this purpose, there are many international associations like the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), the American Association for Clinical Chemistry (AACC) and, the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). According to these, clinical laboratories should measure, monitor, and improve their analytical performances (e.g. internal quality control (IQC) rules, analytical quality specifications, and external quality assessment (EQA) programs in optimum physical conditions, and also control extra-analytic factors that cause pre and post-analytical errors (Plebani et al., 2014). To harmonize and standardize the total testing process (TTP) of the medical labs, the most important step in Turkey is the publication of the Medical Laboratories Regulation (Date: 09.10.2013 Number: 28790). It describes subjects such as the tasks, working principles, physical conditions and licensing of medical labs, assignment of medical staff, supervision or cessation of activities of labs, quality control, lab safety, waste management, lab information system (LIS) and, sample transportation (Tıbbi Laboratuvarlar Yönetmeliği, 2013). According to this regulation, lab directors for biochemistry labs are determined as medical biochemistry specialist who is trained by the medical biochemistry curriculum that complies with Medical Specialty Regulation (Tıpta Uzmanlık Tüzüğü, 2013). The job descriptions of a biochemistry specialist and a medical laboratory technician are also described by the two regulations (Tıpta Uzmanlık Tüzüğü, 2013 and Sağlık Meslek Mensuplarının İş ve Görev Tanımlarına Dair Yönetmelik, 2014). Besides, The Ministry of Health in Turkey has issued many circulars on how to manage and improve the medical laboratories. These can be listed as follows: It is essential that samples of all body fluids except stools and urine are stored under appropriate conditions for at least 24 hours after the result is reported (Tıbbi Laboratuvarlarda Numune Saklama Süreleri, Gözetimli Hizmet Laboratuvarları Kapsamındaki Testler Hakkında Genelge, 2014). The working procedures and principles of

analyzing drugs of abuse/toxicology tests have to be performed at medical laboratories (Yasadışı ve Kötüye Kullanılan İlaç ve Madde Analizi Yapan Tıbbi Laboratuvarlar ile Madde Bağımlılığı Teşhis ve Tedavi Merkezlerindeki Tıbbi Laboratuvarlann Çalışma Usul ve Esasları Hakkında Genelge and 2014 and İdrar Numunelerinde Yasadışı ve Kötüye Kullanılan İlaç ve Madde Analizi Yapan Tıbbi Laboratuvarlar ile Madde Bağımlılığı Teşhis ve Tedavi Merkezlerindeki Tıbbi Laboratuvarların İşleyiş Esasları Hakkında Genelge, 2015). The procedures and principles determined for ethanol analysis in blood samples have to be followed (Tıbbi Laboratuvarlarda Kan Numunelerinde Etanol Analizi İşlemleri Genelge, 2017). The total allowable errors (TEa) and coefficient variations (CV) of the 15 biochemistry parameters have to be calculated at least once a year and not exceed the TEa and CV limits (İzin Verilen Toplam Hata Sınırları, 2016). The Medical Laboratories have to conduct an annual internal and external audit according to licensing criteria stated in the Medical Laboratories Regulation (Tıbbi Laboratuvarlar Yönetmeliği, 2013 and Tıbbi Laboratuvar Yönetmeliği, Tıbbi Laboratuvarların Ruhsatlandırılmasında Kullanılacak Formlar ve Kılavuzlar, 2014). Many other applications have been also activated to improve the safety and quality of medical labs by the Ministry of Health. The Logical Observation Identifier Names and Codes (LOINC) system has been activated in all medical laboratories for standardizing laboratory data (Ministry of Health, 2015). The results of 24 biochemistry tests are sent to the external quality control (EQC) central evaluation system of the Ministry of Health. The "Laboratory Errors Classification System (LECS)" and "Safety Reporting System (SRS)" are generated to use a standard methodology in the analysis of laboratory errors (pre-analytic, analytic, post-analytic) that could threaten patients and healthcare professionals safety. “The undesired event notification system (UENS)” is also uploaded to the HIS of each hospital and used to denounce situations that endanger patients and staff safety. Thanks to the “White code application”, security personal are directed to the scene for people who are exposed to psychological and physical attacks and, a report is created for legal transactions (Ministry of Health, 2021). All documentation related to the Medical Laboratories is created according to the Health Quality Standards Document Management Guide (Ministry of Health, 2020). Quality indicators (QIs) are determined according to Healthcare Quality Standards Indicator

Management Guide (Ministry of Health, 2015). In our country, accreditation of a medical laboratory is voluntary. The medical laboratory can be accredited by the Turkish Accreditation Agency (TÜRKAK) after ensuring compliance with the Turkish Standardization Institute (TS EN)-International organization of Standardization (ISO)/International Electrotechnical Commission (IEC) 17025 and TS EN ISO 15189:2012 standards (TÜRKAK, 2020).

This study aims to show how a biochemistry laboratory in Turkey is managed by national regulations and practices, and thus give the laboratory directors a wider perspective on laboratory management.

2. MATERIALS AND METHODS

The pre-analytical, analytical, and post-analytical processes of our laboratory were evaluated according to the national regulations in Turkey by using the data of the patients who applied to our hospital and the internal and external quality control results of the tests in 2020. Nucleus software was used as the laboratory and hospital information system (LIS/HIS) for data collection, and the Microsoft Excel program was used to analyze the data.

The ethical approval was not requested, since an informed consent was not necessary for the study, and we ensured patient data privacy as in the case of other patient test results stored in our laboratory information system.

3. RESULTS

3.1. Laboratory Design

Diyarbakır Selahaddin Eyyubi State Hospital is a 200-bed capacity hospital, and Biochemistry Laboratory Department has been licensed by the Medical Laboratories Regulation (Tıbbi Laboratuvarlar Yönetmeliği, 2013). It consists of some sections like in any medical laboratory in Turkey: Technical areas (main laboratory areas including support systems such as energy, power supply, water, communication, informatics and, security exterior doors), support areas (at least one sampling, one sample identification and, one material storage areas) and office areas (patient reception, secretariat, toilets, specialist room, and, staff rest area, separated from the technical areas) (Tıbbi Laboratuvarlar Yönetmeliği, 2013).

Among these areas, storage areas are often neglected in many medical laboratories, and it is actually important for laboratories to carry out stock control. The stock control program should be such that the laboratory can closely monitor the status of all medical consumables and reagents, know what quantities are available, and be alert when it needs to be reordered (Turkish Biochemical Society, 2019). In our lab, a technician is responsible for stock control. After the needs of our lab (such as a complete description of the material; the number of packages or item units supplied, approximate monthly usage, priority or importance level of the substance in laboratory work, the time required to receive the delivery, storage space and conditions) have been determined, minimum and maximum stocks are created and these are recorded in the stock forms. The registration regarding the purchase, inspection and storage of materials is made through HBYS. In addition, an inventory system is utilized for all reagents and materials used in all storage areas and in the lab.

We have 3 technical areas: The first is the emergency lab: Emergency biochemistry, emergency cardiac/hormone, arterial blood gases (ABG) and, coagulation tests are analyzed here. The second is the central lab: Routine biochemistry and hormone tests, drug tests in serum, coagulation tests, HbA1c (High-Performance Liquid Chromatography-HPLC method) are measured here. The third is the urine-stool (>7.5 m2) and the urinary drugs of abuse/toxicology (>7.5 m2) laboratories with ventilation systems. The emergency, urine-stool, and urinary drugs of abuse/toxicology labs are open 24/7, and the central lab is open during working hours.

3.2. Laboratory Staff

A total of thirty lab technicians (thirteen in the emergency lab and seventeen in the others) (for sorting, preparation, and analysis of samples, device operation and maintenance, test calibrations, technical test verification, studying of IQCs and EQCs), two secretaries (test requesting, sample identification, and informing the patients and healthcare professionals about TTP), one technic staff for LIS (registering and monitoring test results, errors, QIs and analytic performance requirements electronically), one security guard (for forensic cases at the urinary drugs of abuse/ toxicology lab), two cleaning staff and three biochemistry specialists (one is the lab director) work in our lab. Two

chief technicians (one is for the central lab and the other is for the emergency lab) assist the biochemistry specialists regarding the general functioning of the laboratory. The laboratory director is responsible for everything related to the laboratory and also organizes at least one training program for the staff and self-audit about the lab licensing once a year.

3.3. Laboratory Safety

The biosafety level of our lab is by the physical protection level 2 conditions in the TS EN 12128 standard. There are first aid kit and, safety equipment such as a fire extinguisher and a flame extinguisher cover in the lab. Decontamination and/or neutralization materials are found for chemical and similar injuries, and precautions are taken for their effective use. Personal protective equipment is used by the staff. Staff members are trained on potential hazards at work and safe medical laboratory techniques, and training is recorded. If there is a risk of exposure to infectious agents that cause vaccine-preventable diseases due to the samples, the staff are vaccinated (e.g. Hepatitis). In the medical laboratory technical area, there are a sink and liquid soap for hand-washing and a sterile saline solution (Starline safety, Turkey) for eye washing. The safety documentary created for the lab is easily accessible by the staff. Material safety data sheets of the chemicals are recorded. There are signs and labels on the entrance doors and devices regarding the hazards and risks. Air exchange is provided and controlled access door entry is applied in the lab. The devices and equipment installed for protection in the lab are regularly maintained and checked and recorded. Entry and exit points in the lab are marked. Internationally accepted symbols are used for all signs related to medical laboratory safety and hazards (Tıbbi Laboratuvarlar Yönetmeliği, 2013 and General Directore of Public Health, 2019). Medical waste is decontaminated by the biosafety level of the medical laboratory. Medical laboratory waste management is carried out by the Medical Waste Control Regulation. All electronic systems (LECS, SRS, UENS and, the white code related to lab staff and patient safety are used when necessary. Our hospital complies with the personal data protection policy (General Directore of Health Information Systems, 2019).

3.4. Pre-Pre and Pre-Analytical Phases

International Classification of Disease-10 (ICD-10) codes are entered for all patients by the clinicians before requesting the test (WHO, 2015). The tests are listed under the main test groups as biochemistry, hormone, ABG, coagulation, urine, stool and, emergency tests, with their LOINC and SUT (Sağlık Uygulama Tebliği-Health Practice Statement, 2020) codes. For some tests, test request time limitations are automatically reminded by HIS to the clinicians as determined by the Ministry of Health (Ministry of Health, 2018). For detailed information about the tests and workflow of our laboratory, the biochemistry tests guideline is loaded on the LIS and HIS (Nucleus software, India). There are explanations about the pre-analytical, analytical and, post-analytical phases and estimated turnaround time (TAT) for each test in the guideline (Ministry of Health, 2015). All healthcare professionals can easily access it. The lab director can follow the numbers of tubes and any test information about clinicians and patients on the LIS/HIS.

Test identification is made by the secretary via a bar-coding system. The name of the hospital, patient's first and last name, patient protocol number, tube code, test requesting department, date and time, name and code of the test (as test groups), and cap color of the tube (optional) for the requested test are included in the labels. Samples are taken by phlebotomists with one-use holders and blood collection needles (Becton Dickinson, USA) at blood collection units for outpatients and clinical services for inpatients. Blood taken times are recorded by the phlebotomists via the bar-coding system. Phlebotomists are trained by the lab director about the pre-analytic phase of the tests once a year.

Samples are transported to the laboratory generally by a pneumatic tube system and, rarely by courier service for special situations like an infectious specimen analysis. After transportation, the samples are identified again by the secretary in the lab and are sorted by lab technicians according to test groups. The whole blood specimens in the biochemistry/hormone and coagulation tubes are centrifuged (NF1200; Nüve, Turkey) at 1900x g for 10 minutes at room temperature and 1500x g for 15 minutes at room temperature, respectively. For the drugs of abuse/toxicology analysis, a form is filled, and at least 30 mL urine sample is taken by the patient in a private toilet (with mirrors on each wall and without fountain) under the control of a security guard. After the color

and temperature of the urine sample is evaluated by the technician, the sample is put in two urinalysis tubes and transferred to the adjacent drugs of abuse/ toxicology laboratory (İdrar Numunelerinde Yasadışı ve Kötüye Kullanılan İlaç ve Madde Analizi Yapan Tıbbi Laboratuvarlar ile Madde Bağımlılığı Teşhis ve Tedavi Merkezlerindeki Tıbbi Laboratuvarların İşleyiş Esasları Hakkında Genelge, 2015). National guidelines are taken into account for the pre-analytical phase of all tests in our lab (Turkish Biochemical Society, 2018, 2017). At least once a year, the training about the sample acceptance-rejection criteria is given to all laboratory staff by the lab director. It is recorded on the HIS and repeated after updating every year. Before analysis, each sample is evaluated by technicians according to the LECS (Table 1) and recorded the reasons for the rejected samples on the LIS. Then, these reasons are evaluated, and if necessary, problematic process is reviewed by the lab director. In 2020, our pre-analytical error rates (Number of rejected samples due to pre-analytical error/Total number of samples 100) were low (<1%) for every month.

3.5. Analytical Phase

General biochemistry, some drugs and serum indexes (hemolysis, lipemia, icterus), hormone, HbA1c, ABG, coagulation, urine, fecal occult blood, urinary drugs of abuse/toxicology tests are measured routinely in our laboratory (Table 2). For tests that cannot be analyzed in our lab and rarely requested, we receive testing services from other medical laboratories meeting the necessary conditions (Tıbbi Laboratuvarlar Yönetmeliği, 2013). Technicians carry out cleaning, maintenance, repair, run, and calibrations of devices.

A company staff supports them if necessary. The expiry date control, preparation and stock management of the kits/materials, test calibrations, internal and external quality assessments, detailed algorithms for the testing process, and the verification of the test results are done with the cooperation of the technicians and the biochemistry specialists. The centrifuges, automatic pipettes, and heat-humidity meters are calibrated periodically and posted up-to-date calibration labels on them. Automatic/manual dilutions are defined for the tests above linearity, if possible, on all devices. Method validation/verification and evaluation of measurement uncertainty for quantitative tests are optional (Ministry of Health, 2015 and TURKAK, 2015). All technicians are trained on the safe use of materials and devices before analysis of the tests and operate

each device in rotation. The technicians prepare a file under the supervision of the chief technician and biochemistry specialist for each device, including the user manual or CD, test or device calibration records or certificates, quality control results, device maintenance and failure forms, company contact information, user training certificates. Temperatures for devices such as deep freezer and refrigerator and lab humidity are also monitored by the staff. Lab documents are reviewed at least once a year and revised when there is any change in the TTP (Tıbbi Laboratuvarlar Yönetmeliği, 2013). When there is a change in TTP for any reason (such as device malfunctions, automation problems), the notification is made under the supervision of the biochemistry specialist in the form of a written warning via HIS. The analytical errors are recorded according to LECS (Table 1) for every month, and our analytical error rates (Number of rejected samples due to analytical error /Total number of samples (100) were low (<1%) in 2020.

3.6. Post and Post-Post- Analytical Phases

After the samples are analyzed, test results come to the verification of the technician and lastly the biochemistry specialist. The biochemistry specialist may reject or rerun the tests, based on serum indexes, delta check, or clinical diagnosis. They can also give interpretative comments on tests. Some patient results can also be evaluated in writing and/or by direct communication between the biochemistry specialist and the clinician Health Services General Directorate. The previously determined critical value list Akılcı laboratuvar kullanımı projesi çerçevesinde karar sınırı (eşik değer), kritik değer (panik değer) ve ölçüm birimlerinin harmonizasyonu prosedürü) is introduced to LIS and the critical values (patient's name and last name, protocol number, clinical service, name of the test, critical value result, date and time of test result, notifying person, notified person, notification date and time) are given to the clinician in the form of a color written warning by the technician and/or specialist (if considered necessary, also a verbal warning) before verification of the result. In our lab, critical values notification rates are recorded monthly (Table 4). Manufacturer data is used as the reference interval for each test, and the standards set by the Ministry of Health are used for the decision limits and units (used International System of units). After specialist verifications, each result is reported electronically to the laboratory and hospital information

systems (bi-directional information transfer system). This report contains standard information about the patient, hospital, clinician, biochemistry specialist, laboratory, sample date and time (test requesting, sampling, lab acceptance, and verification), sample type, test (result, status, unit, reference interval/decision limit, last three results) and address information (Health Services General Directorate, 2018). The test report can also be printed on paper. We also notify the number of reported test results every 6 months to the Core Resource Management System (Ministry of Health, 2021). Despite the recommendation of the Ministry of Health, auto verification (Health Services General Directorate, 2018) and reflex/reflective testing (Health Services General Directorate, 2018) cannot be implemented in our laboratory yet, since sufficient electronic infrastructure has not been provided yet.

Samples of all body fluids except stools and urine are stored under appropriate conditions for at least 24 hours after the result is reported (Tıbbi Laboratuvarlarda Numune Saklama Süreleri, Gözetimli Hizmet Laboratuvarları Kapsamındaki Testler Hakkında Genelge, 2014). The backup samples are stored in a deep freezer (-20 °C and below) for ethanol (in gray capped fluoride tubes for blood alcohol testing for 6 months) (Tıbbi Laboratuvarlarda Kan Numunelerinde Etanol Analizi İşlemleri Genelgesi, 2017) and drugs of abuse/toxicology (in urinalysis tube for 6 months) (İdrar Numunelerinde Yasadışı ve Kötüye Kullanılan İlaç ve Madde Analizi Yapan Tıbbi Laboratuvarlar ile Madde Bağımlılığı Teşhis ve Tedavi Merkezlerindeki Tıbbi Laboratuvarların İşleyiş Esasları Hakkında Genelge, 2015). These samples allow the rerun of the test with the reference method if there is clinical suspicion, especially in forensic cases.

The post-analytical errors are recorded according to LECS (Table 1) for every month, and our post-analytical error rates (Number of rejected samples post-analytical error/Total number of samples 100) were low (<1%) in 2020.

Any reports and records about our laboratory are kept for at least thirty years. Electronic records are kept indefinitely with backup. IQC and EQC assessment results are kept in the lab for at least five years, device test calibration results are kept for at least one year (Tıbbi Laboratuvarlar Yönetmeliği, 2013).

3.7. Quality Specifications for TTP

Our laboratory implements quality requirements published by the Ministry of Health. For all tests, IQCs supplied by the manufacturers are studied daily (at least two levels), and EQCs (biochemistry: Bio-Rad, USA; hormone: Bio-Group, Italy; emergency cardiac/hormone: Oneworld Accuracy, Canada; coagulation: Randox, UK; HbA1c: LabPT, Turkey; complete urine analysis: KBUDEK, Turkey; drugs of abuse/toxicology: Oneworld Accuracy, Canada.) are studied monthly. IQC results are automatically transferred to LIS and evaluated by the biochemistry specialists with Levey-Jennings and z-score charts. Results within mean ±2 standard deviations (SD) are generally accepted. Westgard rules are applied by the specialist's discretion. The EQC results of 24 biochemistry tests [amylase (AMY), albumin (Alb), alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), calcium (Ca), chloride (Cl), total cholesterol (T.CHOL), creatinine (Crea), creatinine kinase (CK), direct bilirubin (DBIL), gamma-glutamyltransferase (GGT), glucose (Glc), HbA1c, HDL-cholesterol (HDL), inorganic phosphate (Phos), lactate dehydrogenase (LDH), potassium (K), total protein (TP), total Bilirubin (TBIL), sodium (Na), triglyceride (TG), urea, uric acid (UA)] are sent to the EQC central evaluation system of the Ministry of Health [16]. TEa and total CV of the 15 biochemistry tests (Alb, ALT, ALP, AST, Cl, T.CHOL, Crea, Glc, HDL, LDH, K, TP, Na, TG, urea) are calculated using Microsoft ExcelTM 2010 program (Total $CV=\sqrt{((CV\ level\ 1)^2+(CV\ level\ 2)^2)}$, TEa (%)= Bias% 1.65 total CV%; EQC results are used for bias and IQC results are used for CV) and compared with total CV and TEa limits (İzin Verilen Toplam Hata Sınırları, 2016).These tests are evaluated in our laboratory every month. Since our January results do not exceed the limits, only one month of 2020 was shown (Table 3). Otherwise, it should have been reported every month until improving each result by taking corrective and preventive actions (İzin Verilen Toplam Hata Sınırları, 2016). QIs (Table 4) (Health Services General Directorate, 2020) for our lab are also calculated using LIS and Microsoft ExcelTM 2010 programs every month and recorded on paper and electronically. We calculated the rates for each quality indicator in 2020 (Table 5). We also determined some times for test requesting, sampling, lab acceptance, and verification intervals of samples and compared our test group results with them. Our average test times were within determined target times in 2020 (Table 6).

If the quality assessment results are not suitable for quality standards, a root cause analysis is done. Then, corrective preventive actions for the reasons of nonconformity are carried out and reported. After these activities, the new results are compared with the previous results. For example, we determined the rejected samples monthly with detailed information. The most common reason for rejection was clotted samples that were frequently received for ABG analysis in the emergency department. The second reason is inadequate, and the third one is hemolyzed samples and, these were also seen most frequently in the emergency department. Continuous training of staff for venous blood sampling and continuous monitoring of identification errors using preliminary analytical QIs and direct observation is recommended (Flegar-meštrić and et al, 2016). Therefore, the entire emergency service team was retrained about the pre-analytical phase for all tests. To reduce the number of hemolyzed samples, pneumatic system capsules used in sample transfer were cleaned and, centrifuge time and position were checked. The supervisor inspected the phlebotomists during sampling and, identified and warned the phlebotomist who made a mistake. We also interpreted our panic value notification rates. Although our critical value notification was made (~60%), we tried to increase the notification rates, of course (Piva and et al, 2014). People who did not make the notification were identified, and retrained on how to use the system for critical values. We can give other examples. To activate auto-verification and reflex/reflective test applications in quality indicators, infrastructure studies of the hospital software have been started. After investigating monthly statistics of turnaround times for each test, we noticed that test result times were longer in some services according to our target times (Table 6). We re-examined all steps of the pre-analytical phase for these services and realized that they did not record sampling time accurately. As a result, new barcode readers were purchased and used giving necessary education.

4. CONCLUSIONS AND FUTURE PERSPECTIVE

Medical laboratory management is a difficult and complex process. In this study, we were told about how we managed practically the different stages of the TTP in a medical biochemistry laboratory in TURKEY by national regulations.

As stated in ISO 15189: 2012, medical laboratories should have a dedicated space for the performance of their work designed to ensure

the quality, safety, and effectiveness of the service provided to patients and the health and safety of laboratory staff, patients, and visitors (ISO 15189). In our country, the adequacy of the area reserved for the performance of the work for medical laboratories has been evaluated and determined by the Ministry of Health (Tıbbi Laboratuvarlar Yönetmeliği, 2013). Our laboratory adapts to these conditions. Besides, necessary maintenance and renovations are carried out throughout the year. Successful quality management presumably depends on the ability of laboratories, organizations, and government to collaborate, in addition to the funds and resources available in both the laboratory and the clinical areas. It is also essential to use the advanced systems for the detection and monitoring of the errors that have occurred or will likely occur in each step of all phases in the laboratory as well as the setting up harmonized QIs and performance requirements. Another important point is corrective preventive actions against laboratory errors and harmonization of these actions (Aarsand and Sandberg, 2014). In addition to good analytical measurements made on valid methods and instruments in our laboratory, the development of QIs for laboratory medicine is a fundamental step in providing solid evidence of quality in all procedures and processes of TTP. QIs also play an important role in ensuring targeted continuous improvement activities aimed at reducing the risk of error in clinical practice. Therefore, we took it as our duty to increase the quality of our laboratory by applying the quality indicators determined in our country (Plebani, 2012). The implementation of quality management in medical laboratories in Turkey is continually developing, but it is still not exactly adequate. International standardization requirements such as ISO 15189:2012 will be likely obligations by medical laboratories in the future for Turkey. Because this document identifies the need to ensure quality in every step of the TTP from the pre-pre-analytical phase choosing the right test for the right patient at the right time through analytical steps. reporting the right results in the right form to the post-post-analytical phase giving the right advice and comment on the result (Plebani and et al. 2014). Awareness has been raised with some regulations and applications, but more needs to be done before laboratory staff understands the processes involved, ways of dealing with challenges, and the best ways to implement lab management (Nwaokorie, 2018).

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TABLES

Table 1. Laboratory Errors Classification System List (Ministry of Health, Hata Sınıflandırma Sistemleri)

1.Preanalytical errors	2.Analytical errors
L01. Incorrect test request	L30. Expired kit detection
L02. Missing/incorrect information on test request	L31. Expired material detection
L04. Unregistered sample	L32.The requested material/kit does not arrive
L05. Incorrectly recorded sample	L33. Incorrect material/kit ordered
L06. Sample received from the wrong patient	L34.Material transfer with improper conditions
L07. Misidentified/mislabeled sample	L35. Material stored in improper conditions
L08. Missing sample	L36.Incorrect ambient temperature of the laboratory
L09. Re-sampling	L37. No device maintenance
L10. Incorrect container/tube	L38. Device fault
L11. Empty container/tube	L39. Device pipetting error
L12. Sample in expired tube	L40.Insufficient homogenization of the sample
L13. Unlabeled sample	L41. Inappropriate test procedures
L14. Cancelation of registration because the sample cannot be taken from the patient	L42. Inappropriate performance in EQA
L15 Improperly taken the sample	L43. Working test in inappropriate IQC performance
L16. Insufficient sample volume	L44. Inappropriate IQC
L17. Hemolyzed sample	L45. Inappropriate test procedures
L18. Clotted sample	L47. Incorrect incubation temperature
L19. Lipemic sample	L48. Incorrect incubation time
L20. Icteric sample	L49. Improper staining technique
L22. Unrecorded the sampling time	L50. Inappropriate dilution
L23. Sample not delivered to the laboratory	L51. Inappropriate solution usage
L24. Improper transportation condition	**3.Postanalytical errors**
L25. Excessive transportation time	L52. Incorrect evaluation of the result
L26. Mixing of samples	L53. Incorrect technical test verification
L27. Accepting the sample that needs to be rejected	L54. Data transcription error
L23. Sample not delivered to the laboratory	L55. Incorrect report
L24. Improper transportation condition	L56. Loss of patient outcomes
	L57. Inappropriate turnaround times
	L58. Critical values not reported in a timely manner
	L59. Others

EQA: External quality assesment, IQC: Internal quality control. *This list contains only items that concern the biochemistry laboratory. The laboratory errors mentioned above should be detailed in terms of person, place and time.

Table 2. The General Test Characteristics of Biochemistry Laboratory

Test Groups	Cap color/Tube	Sample	Method	Device
General biochemistry, serum indexes, some drugs and ethanol	Gold/Serum separator tube*	Serum	Photometry, ISE for Na, K, Cl	Architect c16000; Abbott, USA
Hormone	Gold/Serum separator tube*	Serum	Electrochemiluminescence	Cobas 6000; Roche Diagnostics, Germany
Hba1c	Lavender/K2EDTA tube*	Whole blood	High Performance Liquid Chromatography	Adams A1c HA-8160; Arkray, Japan
Coagulation	Light blue/3.2% sodium citrate tube*	Plasma	Photometry	ACL 500; Beckman Coulter, USA
Cardiac/hormone (emergency)	Lavender/K2EDTA tube*	Whole blood	Photometry	AQT90 FLEX, Radiometer, Denmark
ABG	Heparin wash-done injector*	Whole blood	Photometry for Hb ISE for Na, K, Cl Potentiometry for pH,pCO_2 Amperometry for pO_2	ABL 800; Radiometer, Denmark
Drugs of abuse/ toxicology	Urine cup/tube*	Urine	Enzyme multiplied immunoassay technique	Advia 1800; Siemens, Illinois
Complete urinalysis	Urine cup/tube*	Urine	Photometry for chemistry Flow cell for microscopy	UriSed; 77 Elektronika Kft, Hungary
FOB	Stool Cup*	Stool	Immunochemistry	True Line; Biocare diagnostic,-Chine

Calculated tests	Corrected calcium Creatinine clearance eGFR (CKD-EPI 2012) Globulin HOMA-IR index Indirect bilirubin LDL-cholesterol (Friedewald formula) Non-HDL-cholesterol Protein/albumin/creatinine/electrolytes in 24-hour urine PT-INR Total Iron Binding Capacity Transferrin saturation (%) VLDL-cholesterol

ABG: Arterial blood gases, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, Cl: Chloride, eGFR: estimated glomerular filtration rate, FOB: Fecal occult blood, Hb: Hemoglobin, HOMA-IR: Homeostatic Model Assessment-Insulin Resistance, ISE: Ion-Selective Electrode, K: potassium, Na: Sodium, PT-INR: Prothrombin time- International normalized ratio.

*BD Vacutainer blood/urine collection cups/tubes (Becton Dickinson, USA)

Table 3. Total Allowable Errors (TEa) and Total Coefficient Variations (CV) of the 15 Biochemistry Tests in January 2020

Tests	Calculated TEa (%)*	Calculated Total CV (%)**	Turkey TEa (%)	Turkey Total CV (%)
Alb	14.4	7.0	15	7.5
ALT	17	7.0	20	10
ALP	10.8	6.1	30	10
AST	11.2	4.7	20	10
Cl	4.9	2.7	9	5
T.CHOL	10.1	5.5	11	5
Crea	15.3	6.6	20	10
Glc	7.8	3.1	11	5
HDL	24.8	7.9	30	10
LDH	14.0	7.6	21	10
K	7.4	4.0	9	5
TP	9.5	5.3	15	7.5
Na	6.0	3.0	9	5
TG	13.7	5.7	15	7.5
Urea	12.0	5.6	15	7.5

Alb: Albumin, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, AST: Aspartate aminotransferase, Cl: chloride, T.CHOL: Total cholesterol, Cre: Ceatinine, Glc: Glucose, HDL: High-density cholesterol, LDH: Lactate dehydrogenase, K: Potassium, TP: Total protein, Na: Sodium, TG:Triglyceride.

*(%)= Bias% + 1.65 x total CV%

**Total CV=$\sqrt{((CV\ level\ 1)^2 + (CV\ level\ 2)^2)}$; external quality control result (n=1 for each test) is used for bias

Internal quality control results (n≥20 for each level of control) are used for CV (Ministry of Health, İzin verilen toplam hata sınırları).

Since our January results do not exceed the limits, only one month of 2020 was shown. Otherwise, it should have been reported every month until improving each result by taking corrective and preventive actions (Ministry of Health, İzin verilen toplam hata sınırları).

Table 4. Quality Indicators for a Turkish medical biochemistry laboratory

1. Rejected Sample Rate in Biochemistry Laboratory Tests= Number of rejected samples / Total number of samples x 100 (every 3 months)
2. Rate of Sample Lost in Biochemistry Laboratory Process= (Number of samples lost / Total number of samples) x 100 (every 3 months)
3. Number of Nonconformities in Biochemistry Laboratory IQC Studies= The number of nonconformities detected in the IQC studies in the biochemistry laboratory on the test basis (every 3 months)
4. Number of Nonconformities in Biochemistry Laboratory EQA Studies= Number of tests with nonconformity reported in external quality assessment studies in the biochemistry laboratory (every 3 months)
5. Rational Laboratory* Compliance Rate in Biochemistry Laboratory= (The number of working steps in the rational laboratory use that was adapted / Total rational laboratory use number of working steps) x 100 (every 6 months)
*Rational laboratory use working steps:
a. Rational test request procedure (Health Services General Directorate, 2018)
b. Consultation request procedure (Health Services General Directorate, 2018)
c. Auto-verification system usage procedure (Ministry of Health)
d. Reflex and reflective test applications (Ministry of Health)
e. Harmonization of decision limits, critical values, and measurement units (Health Services General Directorate, 2018)
f. Medical laboratory patient test result report standardization (Ministry of Health)
g. Recording test list of each laboratory on a common system in Turkey (Which lab can analyze this test ?) (Ministry of Health)

IQC: Internal quality control, EQA: External quality assessment.

Table 5. Critical Values Notification Rates and Quality Indicators Results in 2020

	Critical values notification rates (%)	Rejected Sample Rates (%)	Lost Sample Rates (%)	Rational Laboratory Compliance Rates* (%)	Number of Nonconformities in IQCs	Number of Nonconformities in EQA
January-March	62.1	0.45	<0.01	0.71	708 (3.66%)	19 (4.42%)
April-June	53.1	0.92	0	0.71	382 (2.92%)	18 (4.86%)
July-September	66.9	0.78	0	0.71	413 (2.61%)	16 (4.12%)
October-December	72.2	0.82	<0.01	0.71	298 (1.8%)	13 (3.2%)

EQA: External quality assessment, IQC: Internal quality control. *5 (a,b,f,e,g) of the 7 (a,b,c,d,e,f steps can be practically implemented (See Table 4).

Table 6. Target and Average Times of Tests in 2020

Test Groups	Target times(minute)		Average times (minute)	
	A	B	A	B
General biochemistry	60	120	36	54
General biochemistry (emergency)	60	60	30	32
Hormone	60	180	58	180
Hba1c	60	180	52	142
Coagulation	60	60	25	54
Cardiac/hormone (emergency)	30	30	10	29
ABG	30	15	11	6
Drugs of abuse/ toxicology	60	60	54	52
Urinalysis	60	60	29	16
FOB	60	60	25	10

A: Sampling-lab acceptance, B: Lab acceptance-result verification, ABG: Arterial blood gases, FOB:Fecal occult blood.