World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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# Verification of analytical performance of DHEA assay on the Abbott Architect ci8200: Experience of the biochemistry laboratory Mohammed VI Oujda

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World Journal of Biology Pharmacy and Health Sciences, 2024, 19(02), 254–260

Publication history: Received on 26 June 2024; revised on 09 August 2024; accepted on 12 August 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.19.2.0503

## Abstract

**Introduction:** Dehydroepiandrosterone sulfate (DHEA-S) is the main adrenal androgen produced by the adrenal cortex and also acts as a neurosteroid. DHEA-S is an excellent indicator of adrenal androgen production. Although DHEA-S has low androgenic potency, it metabolizes into more potent male hormones such as testosterone and androstenedione.

**Objectives:** This work describes the verification/validation procedure for the biological parameter dehydroepiandrosterone sulfate (DHEA-S). This procedure is one of the main and constant concerns of biologists in quality management, aiming to produce fair and reliable measurements. Based on the recommendations of the protocol from the technical guide for accreditation in human health, SH GTA of COFRAC according to ISO 15189, we performed the verification of a microparticle immunoassay method by chemiluminescence (CMIA) for the quantitative determination of dehydroepiandrosterone sulfate (DHEA-S) in human serum and plasma on the Architect system.

**Results and Discussion:** The verification of criteria (repeatability, reproducibility) was conducted using routine samples from patients hospitalized at the university hospital and internal and external quality controls. The study of analytical performance showed the conformity of repeatability with the supplier's coefficients of variation (CVs) and data from learned societies (RICOS). The results obtained for intra-laboratory reproducibility were satisfactory for level 1 with a CV of 7.85% and quite satisfactory for levels 2 and 3 with a CV of 4.63% and 4.26%, respectively.

**Conclusion:** In conclusion, the automated system can be considered suitable for medical laboratories due to its analytical performance in the determination of common biochemical parameters. In addition to laboratory staff, equipment, and environmental factors, the accuracy and reliability of results obtained during an examination are also influenced by the methods and any subsequent validation or verification.

**Keywords:** Dehydroepiandrosterone sulfate (DHEA-S); Adrenal androgens; Chemiluminescence immunoassay (CMIA); Analytical performance; Quality management

## 1. Introduction

Dehydroepiandrosterone sulfate (S-DHEA) is the primary adrenal androgen produced by the adrenal cortex and also functions as a neurosteroid. It serves as an excellent marker for adrenal androgen production. Although S-DHEA has low androgenic potency, it can metabolize into more potent male hormones such as testosterone and androstenedione. Serum concentrations of S-DHEA decrease with age and can serve as prognostic indicators for the progression of serious diseases and breast cancer [1]. Elevated levels of S-DHEA are observed in the plasma of patients with adrenal tumors

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or congenital adrenal hyperplasia, and may also be slightly elevated in patients with polycystic ovary syndrome. In men, hCG-producing tumors can lead to elevated S-DHEA levels originating from the testes [2].

The determination of dehydroepiandrosterone sulfate (S-DHEA) is crucial, requiring precise and reliable tests for diagnostic and therapeutic monitoring. It is a primary assay for investigating hirsutism and virilism in women and girls, and is also recommended for children to demonstrate premature adrenal maturation. Additionally, it is prescribed for elderly individuals as S-DHEA production gradually declines with age in both men and women [3].

The method used to determine S-DHEA in medical biology laboratories must be verified in accordance with established standards, such as ISO 15189, to ensure reliable results. The verification process involves quality control measures, calibration, and comparison of results with established reference methods. This process identifies and addresses potential sources of error, validates method performance, and ensures consistent, accurate results. Adherence to ISO 15189 ensures the precision and accuracy of the S-DHEA assay, enhancing the quality of patient care. [4]

Verification of an analytical method is essential for ensuring that results are as close as possible to the true reference value of a sample. Accurate and reliable S-DHEA measurements are critical for accurate diagnosis, appropriate therapeutic decisions, monitoring disease progression, and improving patient care, whereas inaccurate results can lead to serious consequences, including misdiagnosis and inappropriate treatment [5].

In our study, we conducted an analytical evaluation of the S-DHEA serum assay using a kit on the ARCHITECT 8200 system in the biochemistry laboratory of CHU Mohammed VI in Oujda.

### 1.1. Reminder on DHEA

Dehydroepiandrosterone (DHEA) is synthesized from cholesterol in all steroidogenic tissues: ovaries, testes, and the adrenal gland (reticular zone). The conversion of DHEA-to-DHEA sulfate (S-DHEA) occurs in the adrenal gland and peripheral tissues, mainly the liver. S-DHEA can also be synthesized from cholesterol sulfate via a sulfate pathway, where all intermediates are sulfates. While DHEA is mainly secreted by the adrenal cortex and partly by the gonads, S-DHEA is exclusively secreted by the adrenal cortex [2].

DHEA has a lower androgenic potency compared to testosterone. Both DHEA and S-DHEA circulate in the blood, primarily bound to albumin. DHEA has a half-life of approximately 30 minutes, whereas S-DHEA has a half-life of around 10 hours. DHEA and S-DHEA are in reversible equilibrium through the action of sulfotransferases and sulfatases, mainly in the liver and kidneys. The sulfo-conjugated product is primarily excreted unchanged in the urine [1].

A key characteristic of S-DHEA is the change in its plasma levels over a lifetime. Adrenarche, occurring around ages 8-9, is marked by an increase in adrenal androgens, particularly S-DHEA. Plasma levels peak between ages 15 and 45, then decline, reaching their lowest levels after age 60. Thus, aging is associated with decreased S-DHEA levels. Moderate increases in S-DHEA in women have unclear pathological significance. Conversely, extremely low plasma S-DHEA concentrations are seen in primary adrenal insufficiency and pituitary insufficiency with corticotropic deficiency [2].

Reduced DHEA levels are thought to trigger diseases due to its role in stimulating immune defenses against infections and certain viruses like herpes. It reduces the onset of age-related diseases such as cancer and coronary heart disease, prevents adult-onset type II diabetes, facilitates weight loss, improves conditions for patients with Alzheimer's, lupus, HIV, and chronic fatigue, alleviates menopause and depression symptoms, improves memory and learning, and increases life expectancy [1].

## 2. Materials and Methods

### 2.1. Principle of the Assay Method

The ARCHITECT (DHEA-S) assay is a chemiluminescence microparticle immunoassay (CMIA) for the quantitative determination of dehydroepiandrosterone sulfate (S-DHEA) in human serum and plasma on the ARCHITECT system. The assay principle involves mixing the sample, assay diluent, and paramagnetic microparticles coated with anti-S-DHEA antibodies. The S-DHEA in the sample binds to the antibody-coated microparticles. After incubation, an acridinium-labeled S-DHEA conjugate is added, binding to the free sites on the microparticles. Following further incubation and washing, pre-activation and activation solutions are added. The resulting chemiluminescent reaction is measured in relative light units (RLU), with an inverse relationship between the S-DHEA concentration and the detected RLU [6].

### 2.2. Verification Procedure

Verification of analytical methods involves assessing the method's performance according to a standardized protocol, evaluating it against standards set by learned societies (RICOS, FSCB), and ensuring sufficient performance for accurate clinical interpretations. This descriptive study was conducted over 30 days in the biochemistry laboratory of CHU Mohammed VI in Oujda, following the COFRAC GTA 04 certification technical guide protocol [7].

Dehydroepiandrosterone sulfate was tested on the ARCHITECT 8200c automated chemiluminescence analyzer (CMIA) to assess analytical performance in terms of repeatability and reproducibility using patient samples and internal quality controls. Data were statistically processed using BYG informatics' EVM middleware module, comparing coefficient of variation (CV) values with those established by learned societies (RICOS) and the supplier's data.

## 3. Results

The results showed satisfactory repeatability for the Abbott Architect ci 8200 at low, medium, and high levels, with coefficients of variation (CV) of 5.65%, 2.42%, and 1.84%, respectively. Intra-laboratory reproducibility was also satisfactory for levels 1, 2, and 3, with CVs of 7.85%, 4.63%, and 4.26%, respectively. These results meet the criteria of the RICOS protocol for repeatability and intra-laboratory reproducibility**.**

**Table 1** Repeatability results for DHEA on Architect ci8200 automaton

| SAMPLE | N | MEANS | SD | CV % | CV SUPPLIER% | CV RICOS |
|---|---|---|---|---|---|---|
| LEVEL 1 | 30 | 9.40ug/dl | 0.531ug/dl | 5.65% | 5.24% | 6.53% |
| LEVEL 2 | 30 | 104ug/dl | 2.518ug/dl | 2.42% | 2.38% | 6.53% |
| LEVEL 3 | 30 | 969.99ug/dl | 17.88ug/dl | 1.84% | 2.68% | 6.53% |

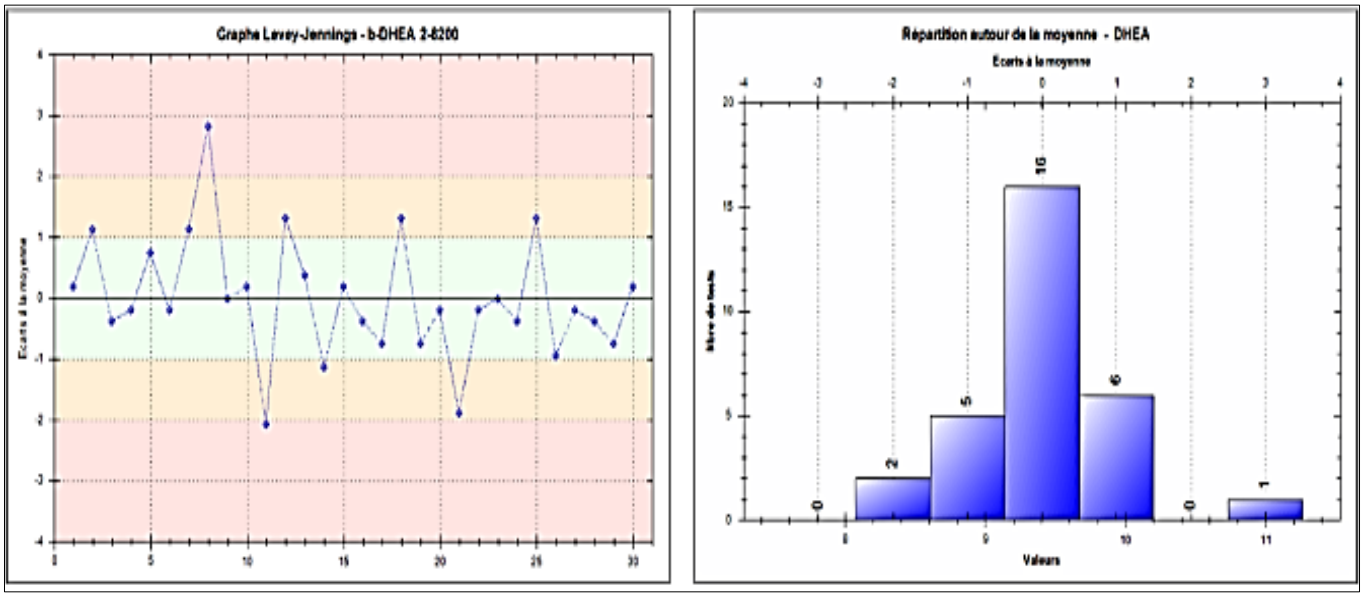


**Figure 1** Low level of repeatability, Levey Jenning graph and the distribution around the mean

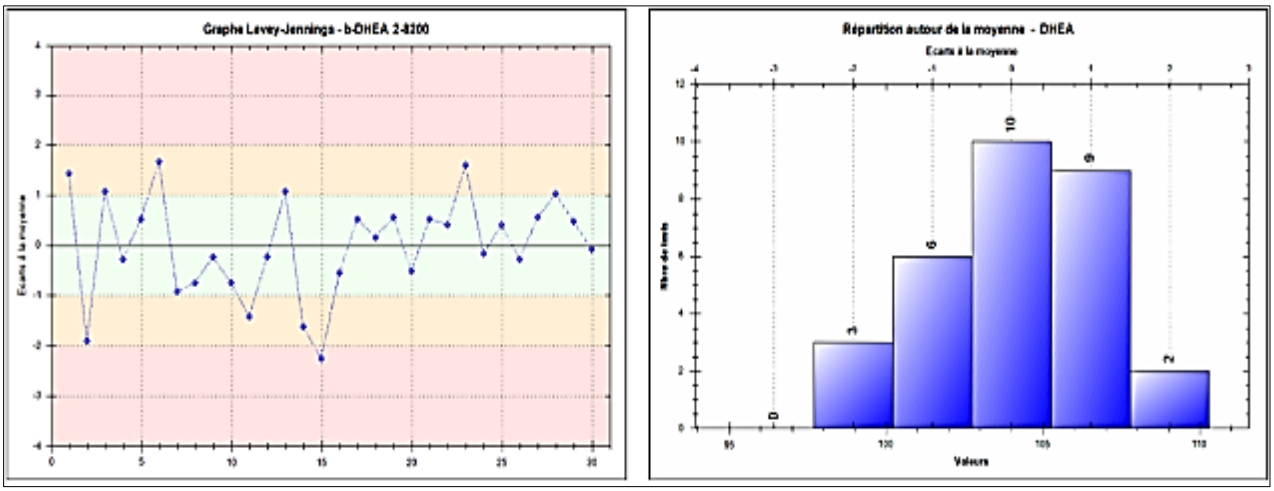


**Figure 2** Medium level of repeatability, Levey Jenning graph and the distribution around the mean

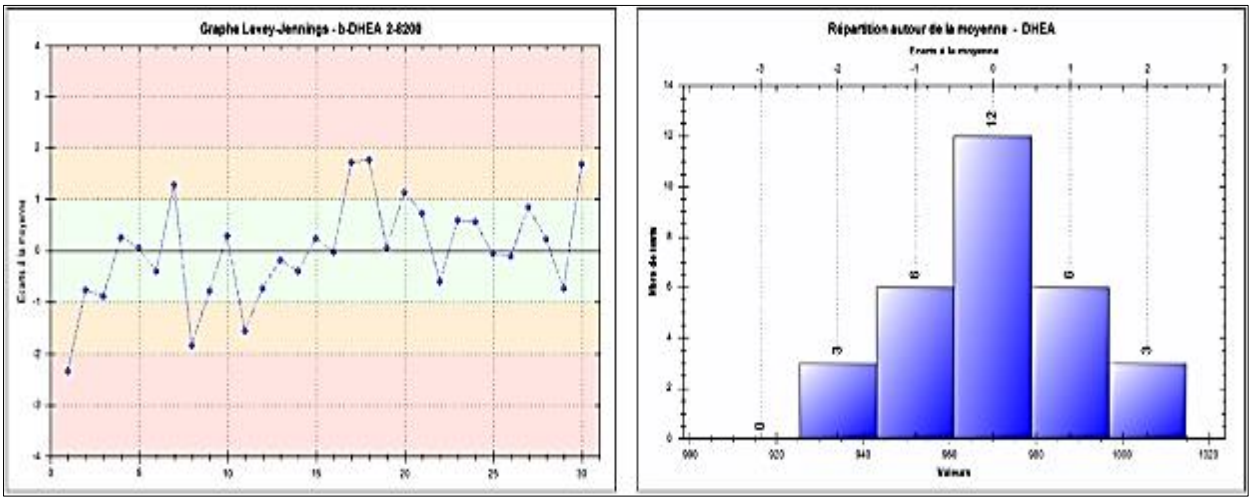


**Figure 3** High level of repeatability, Levey Jenning graph and the distribution around the mean

**Table 2** Reproducibility results for Sodium on Architect ci8200 automaton

| SAMPLE | N | MEAN (µg/dl) | SD | CV% | CV SUPPLIER% | CV RICOS% |
|---|---|---|---|---|---|---|
| LEVEL 1 | 30 | 33.06 | 2.6 | 7.85 | 7.41 | 30.7 |
| LEVEL 2 | 30 | 194.55 | 9.004 | 4.63 | 4.68 | 30.7 |
| LEVEL 3 | 30 | 20.75 | 20.75 | 4.26 | 4.93 | 30.7 |

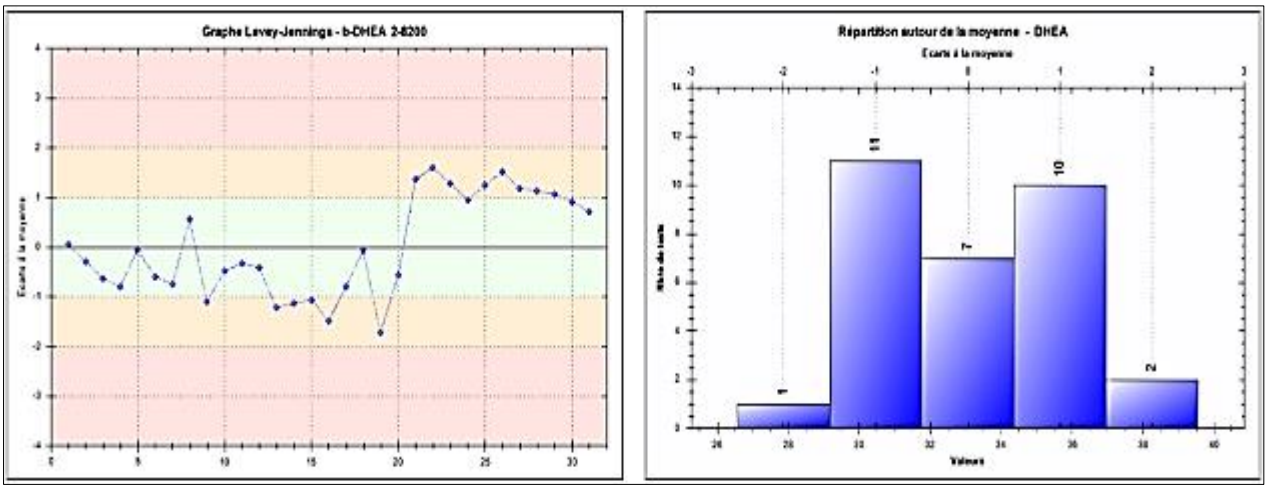


**Figure 4** Low level of reproducibility, Levey Jenning graph and the distribution around the mean

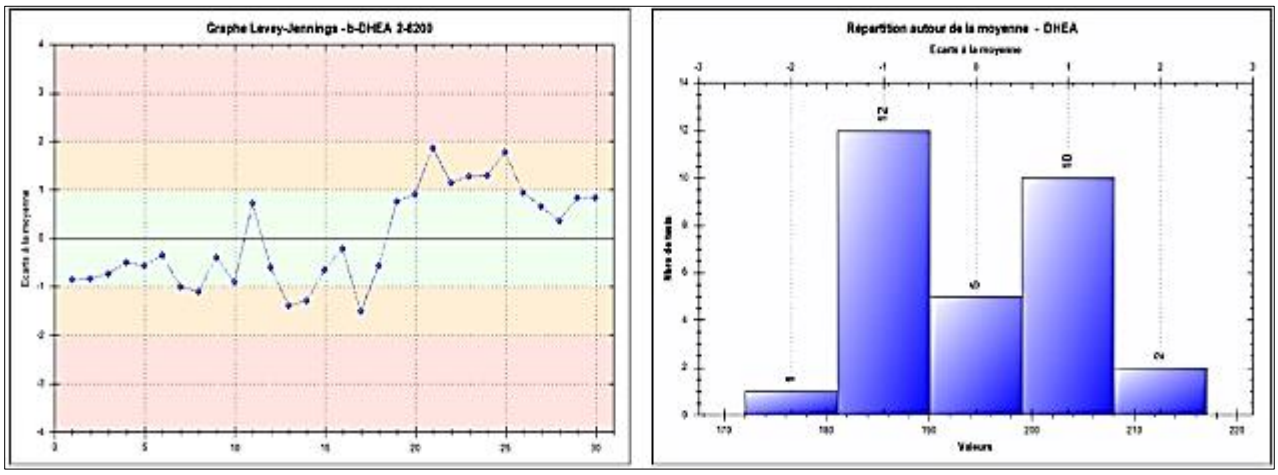


**Figure 5** Medium level of reproducibility, Levey Jenning graph and the distribution around the mean

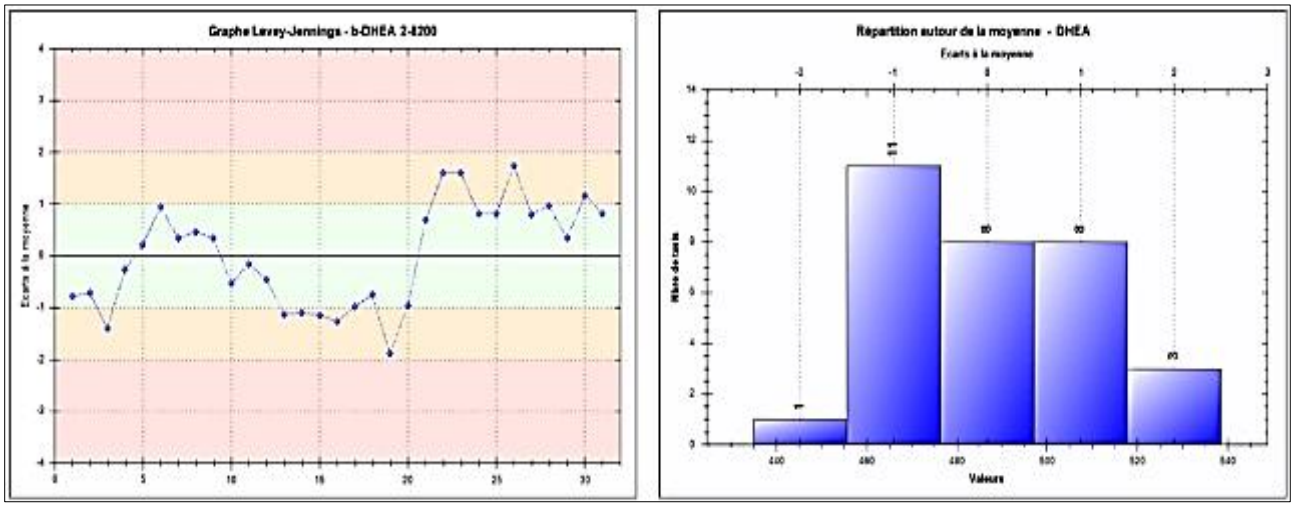


**Figure 6** High level of reproducibility, Levey Jenning graph and the distribution around the mean

## 4. Discussion

The recognized methods have been validated in their respective fields of application as part of our "verification/validation scope A" approach. Abbott biochemistry methods, marked with the CE certification, are approved for use in clinical diagnostics in medical biology. Consequently, these techniques fall under the flexible A category for method verification, which can be conducted following the COFRAC guide SH-GTA-04. This approach allows for method verification within laboratory procedures, rather than requiring a full method validation. Therefore, there is no need to confirm the technique's sensitivity and specificity, reagent stability, robustness, or to compare it with a reference method [8].

For the parameter under evaluation, repeatability assessment ensures optimal performance conditions and confirms the proper functioning of the system, including instruments and reagents. Reproducibility evaluates the method's consistency across various variables, such as different operators, time points, reagent batches, and calibrations. Correct and appropriate interpretation of results necessitates critical reading, focusing on the clinical significance of the results while considering their representativeness and the biological variations, which may differ in importance from one compound to another [9].

The primary goal of method verification/validation is to understand the method's limitations and its relevance to clinical applications. Overall, the coefficients of variation obtained from the intra-laboratory repeatability and reproducibility studies are excellent, meeting both the protocol criteria (RICOS) and the supplier's standards. Creating a verification/validation technical file is essential for any medical analysis laboratory seeking ISO 15189 accreditation [4,9]. The repeatability and reproducibility of the S-DHEA parameter were assessed and found to be satisfactory.

## 5. Conclusion

In conclusion, the automated system is suitable for medical laboratories due to its strong analytical performance in determining common biochemical parameters. The accuracy and reliability of results obtained during examinations are influenced not only by laboratory staff, equipment, and environmental factors but also by the methods used and their subsequent validation or verification.

The Biochemistry Laboratory at CHU Mohammed VI d'Oujda, a leading healthcare facility in the eastern region of Morocco, has adopted a quality strategy that includes a method verification process. Completing this study will facilitate the reliable establishment of an accreditation process for analyses conducted in our laboratory. As a reference center in the Eastern region of Morocco, the laboratory not only manages referred or hospitalized patients but also assesses the health status of the general population through various scientific studies.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors declare no conflict of interest.

### *Funding Sources*

This research did not receive any specific funding from public, commercial, or non-profit funding agencies.

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