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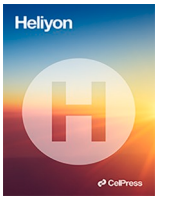

High-sensitive detection and quantitation of thyroid-stimulating hormone (TSH) from capillary/fingerstick and venepuncture whole-blood using fluorescence-based rapid lateral flow immunoassay (LFIA)

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ABSTRACT

Background: In the last decade, point of care testing (POCT) such as lateral flow immunoassays (LFIA) were developed for rapid TSH measurement. Most of these TSH-LFIAs are designed for qualitative measurements (i.e., if TSH values > 5, or >15 IU/L) and as screening tests for primary hypothyroidism in children and adults. Serum or plasma, but not venepuncture whole-blood or fingerstick/capillary, are usually used to quantify TSH accurately. Studies on performance evaluation of TSH-LFIAs POCT using venepuncture or fingerstick whole-blood are limited. Additionally, limited studies evaluated the performance and validity of TSH-LFIAs POCT compared to valid and reliable reference methods. To our knowledge, this is the first study to evaluate three different blood withdrawal techniques for evaluating POCT of TSH.

Aim: We aim to evaluate the performance of a new fluorescence-based LFIA and its Finecare™ fluorescent reader for quantitative measurement of TSH from a fingerstick, venepuncture whole-blood, and serum.

Methods: 102 fingerstick, venepuncture whole-blood, and serum samples (with normal and abnormal TSH values) were analyzed by Finecare™ Rapid Quantitative LFIA test and Roche cobas® e 601 as a reference test.

Results: Using serum, when compared to cobas® e 601 reference method, Finecare™ showed high sensitivity [90.5 % (69.6–98.8)] and specificity [96.3 % (89.6–99.2)] for diagnosis of thyroid abnormalities (<0.35 or >4.5 mIU/L). The actual test values (mIU/L) of Finecare™ showed

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excellent agreement (Cohen's Kappa = 0.85) and strong correlation (r = 0.93, p < 0.0001) with cobas® e 601. Using venepuncture whole-blood samples, Finecare™ showed similar results to serum with high sensitivity [95.2 % (76.2–99.9)], specificity [97.5 % (91.4–99.7)], excellent agreement (Cohen's Kappa = 0.91), and very strong correlation (r = 0.95, p < 0.0001) with cobas® e 601. These results suggest that Finecare™ can be used for quantitative measurement of TSH using serum or venepuncture whole-blood. These key performance indicators were slightly decreased when fingerstick whole-blood samples were used: sensitivity [85.7 %(63.7–97)], specificity [90.0 %,(81.5–96)], good agreement (Cohen's Kappa = 0.7) and very strong correlation (r = 0.9, p < 0.0001) with cobas® e 601. A subgroup analysis of abnormal TSH samples revealed a strong and significant correlation between the reference, Finecare™ whole-blood (r = 0.692; p = 0.0015), and fingerstick test Finecare™ (r = 0.66; p = 0.0025). A very strong correlation was also observed between cobas® e 601 serum and Finecare™ serum (r = 0.88; p < 0.0001). Conclusion: In comparison to the reference assay, our study demonstrates that Finecare™ exhibits high sensitivity, specificity, agreement, and a strong correlation. These findings provide evidence that Finecare™ is a reliable, valid, and accurate point-of-care test for TSH screening and quantitative measurement, especially in non- or small laboratory settings.

1. Introduction

Endocrine and metabolic disorders are common worldwide [1–3]. Among these, thyroid dysfunction remains a major problem [1]. The measurement of thyroid-stimulating hormone (TSH) levels represents the first-line assay for assessing thyroid function [2]. TSH is the most significant test for understanding any relevant thyroid problems [3]; along with triiodothyronine (T3) and thyroxine (T4) testing, primary or secondary thyroid disease can be diagnosed [4].

TSH reference range values are affected by age and gender [5]. However, according to the literature, the normal/reference range for male and female adults is generally between 0.35 and 4.5 mIU/L [3,6,7]. Values above 4.5 mIU/L indicate low thyroid function (hypothyroidism), and values less than 0.35 mIU/L indicate hyperactive thyroid [8,9]. The frequency of thyroid dysfunction cases dictates the need for skilled physicians to diagnose thyroid diseases [6]. Another prerequisite for thyroid dysfunction diagnoses and follow-up treatments is to provide reliable analytical equipment for testing thyroid-related hormones. Because TSH is the first-line test to screen or confirm thyroid disease, equipment with high sensitivity and specificity is always needed to reduce the incidence of false diagnoses. Failure to assess thyroid dysfunction puts the patient at high risk for different conditions, such as infertility, osteoporosis, and cardiovascular disease [7].

Immunoradiometric assay (IRMA) is considered the most sensitive assay and a reference method for quantitative measurement of many analytes and hormones, including TSH [10]. Due to many limitations of the IRMA, the third generation fully automated chemiluminescence or electrochemiluminescence immunoassays (CLIA or ECLIA) became the most popular and sensitive assays to measure hormones [11–13]. For instance, the Elecsys' fully automated ECLIA system, such as Cobas, which developed by Roche, is now considered one of the most reliable systems for analyzing TSH with clinical suspicion of thyroid disease [11–13].

The demand for rapid measuring of results (e.g., in intensive care and newborn screening) and the development of a testing method that can also be operated, by nursing staff, with minimal cost are factors contributing to the increasing use of point-of-care testing (POCT) equipment. While comparable with conventional laboratory assays (ELISA and CLIA) in terms of sensitivity and specificity, the POC tests, such as lateral flow immunoassays (LFIAs) save time and reduce costs [14]. Recently many commercial LFIAs for measuring TSH were developed by different manufacturers. However, most of these LFIAs are mainly used for screening primary hypothyroidism in children (only detects values more than 5 mIU/L) and are not approved in the USA or Europe [15]. The issues with those methods are the lack of sensitivity and accuracy and that they cannot measure a wide range of readings. Additionally, most LFIA use plasma or serum, which requires extensive processing and trained personnel to handle the blood withdrawal and sample preparation for analysis [15].

In the last 15 years, many LFIAs were developed and proposed for quantitative measurement of TSH [16,17].However, their performance remains to be compared to a standard and reliable laboratory assay. Therefore, in the present study, we aim to evaluate the performance of the Finecare™ TSH Rapid Quantitative Test using samples obtained from fingerstick/capillary, venepuncture whole-blood and serum. We used the Elecyes system Roche cobas® e 601 ECLIA analyzer from Roche Diagnostics as a reference method for this evaluation. In addition, we aim to evaluate the effect of using different type of samples (serum, fingerstick and whole-blood) on Finecare™ TSH quantitative results.

2. Materials and methods

2.1. Sample collection and ethical approval

In this study, a 102 fingersticks/capillary and matched venepuncture whole-blood, and serum samples were collected from participants visiting a clinical laboratory in Jordan. All participants, with known thyroid problems, visited the clinical laboratory to recheck their TSH values. Participants were monitored for other medical conditions that would influence TSH results. Among all participants, only one participant reported the presence of thyroid carcinoma.

Since recruiting participants in a short period is very challenging, we used a minimal sample size that can generate a reliable statistical analysis. Thus, we relied on similar and previously conducted articles studies to estimate the sample size of our study [2, 18–22]. An estimated sample range of 100–150 was deemed sufficient to estimate the performance evaluation of POCT of TSH in comparison to a reference standard.

Data were collected in 2022. Ethical approval was granted for data collection by Qatar University (IRB#. QU-IRB 1766-E/22), Reviewed by Qatar University Institutional Review Board QU-IRB.

2.2. Finecare™ TSH rapid quantitative test

The Finecare™ TSH relies on a solid sandwich immunodetection method to rapidly quantify TSH. Fingerstick or EDTA whole-blood and serum samples were processed following the manufacturer's recommendations. The venepuncture whole blood was collected using standard phlebotomy techniques. A total of 5 mL of whole blood was withdrawn from the median cubital vein. The collected whole-blood specimen was added to the collection tube containing the recommended EDTA anticoagulant. Samples were then centrifuged for 10 min to separate the serum from the blood.

Following blood collection, samples were immediately tested on Finecare™ to reduce the possibility of coagulation. The samples that showed blood clots were repeated and then included in the analysis.

A sample of 75 μL of the whole blood/serum was taken for testing on the Finecare™ FIA meter. Using a transfer pipette, the 75 μL were withdrawn and added to the buffer tube mix the sample mixture thoroughly by shaking it about 10 times. The mixture was then loaded into the sample well of the test device. The sample was inserted into the sample holder of the Finecare™ FIA meter. The reaction time was 15 min. The deviations beyond the reference range of 0.35–4.5 mIU/L were considered positive [23].

2.3. Reference method Roche cobas® e 601

The cobas® 6000 analyzer series cobas® e 601 module is a fully automated analyzer that uses a patented electrochemiluminescence (ECL) technology for immunoassay analysis. The Elecsys® Anti-TSHR test uses anti-human THS monoclonal antibodies labelled with ruthenium complex. The test follows a sandwich principle and takes around 18 min for the complete execution. All samples were processed following the manufacturer's recommendations. The specimens were placed in collection tubes containing the EDTA anticoagulant, the same tubes that were used for the samples collected for testing on Finecare™. Briefly, 50 μL of the patient's sample was incubated with the TSH- specific monoclonal antibody labelled with a ruthenium complex, which will react to form a sandwich complex. After that, streptavidin-coated microparticles were added, and samples were incubated. During the incubation, the complex binds to the solid phase via biotin and streptavidin interaction. The reaction mixture is added to the measuring

Table 1
Participant characteristics.

Age (years)	38.92 ± 15.83
Gender	
Males	36 (35.3)
Females	66 (64.7)
Results of serum Finecare™	
Normal TSH levels	78(76.5)
Hypothyroidism	20(19.6)
Hyperthyroidism	4(3.9)
Average result of serum Finecare™ (mIU/L)	4.27 ± 10.09
Results of whole-blood Finecare™	
Normal TSH levels	83(81.4)
Hypothyroidism	17(16.7)
Hyperthyroidism	2(2.0)
Average result of whole-blood Finecare™ (mIU/L)	4.85 ± 14.21
Results of fingerstick Finecare™	
Normal TSH levels	82(80.4)
Hypothyroidism	18(17.6)
Hyperthyroidism	2(2.0)
Average result of fingerstick Finecare™ (mIU/L)	4.56 ± 10.84
Results of cobas® e 601	
Normal TSH levels	81 (79.4)
Hypothyroidism	20 (19.6)
Hyperthyroidism	1(1.0)
Average result of cobas® e 601 (mIU/L)	4.71 ± 10.67

Categorical variables were reported as frequency and percentage [n (%)]; continuous variables were reported as mean ± standard deviation.

cell, so the microparticles are captured into the electrode surface by magnetic attraction. Following the additions of ProCell M solution to remove the unbound substances, a voltage is applied to the electrode, which induces chemiluminescent emission measured by a photomultiplier.

2.4. Statistical analysis

Data were analyzed using GraphPad Prism 9.3.1 (San Diego, CA, USA). The collected dataset was subjected to the Shapiro-Wilk normality test to evaluate data normality. In the absence of normal distribution, non-parametric tests were performed using Kruskal-Wallis to test for the differences between independent samples. p-values $\leq$0.05 were considered statistically significant.

Using Roche cobas® e 601 as the reference standard, concordance analysis based on 2x2 contingency tables was conducted. These concordance measures included overall percentage agreement (OPA), positive (PPV), and negative predictive values (NPV), as well as Cohen's Kappa statistics. Those measures were previously used in assessing the performance of Finecare™ [18,24]. The latter measure is a standard and robust metric that estimates the level of agreement, beyond chance, between two diagnostic tests. Ranging between 0 and 1, a Cohen's Kappa value $<$ 0.40 denotes poor agreement, 0.40–0.59 denotes fair agreement, 0.60–0.74 denotes good agreement, and $\geq$0.75 denotes excellent agreement [25]. The significance level was indicated at 5 %, and a 95 % confidence interval (CI) was reported for each metric. Correlation and linear regression analysis were performed between FinecareTM and the reference method, and between FinecareTM's different blood draws. Spearman correlation coefficient (r) was calculated. For absolute values of spearman's r, 0–0.19 is denoted as a very weak correlation, 0.2–0.39 as weak, 0.40–0.59 as moderate, 0.6–0.79 as strong, and 0.8–1 indicates a very strong correlation. Confidence interval (CI) at 95 % were indicated for all tests [26].

3. Results

3.1. Participant characteristics

A total of 102 fingerstick, matched venepuncture whole-blood, and serum samples were collected from participants. The average age of the participants was 38.92 $\pm$ 15.83 years, and the majority were females [66(64.7 %)] (Table 1). Most of the participants had normal TSH levels on the reference method cobas® e 601 [81(79.4); 4.71 $\pm$ 10.67 mIU/L]. Similarly, results of the venepuncture serum [78(76.5 %)], whole-blood [83(81.4 %)], and fingerstick [82(80.4 %)] on Finecare™ revealed that the majority of participants had normal TSH values (4.27 $\pm$ 10.09 mIU/L, 4.85 $\pm$ 14.21 mIU/L, and 4.56 $\pm$ 10.84 mIU/L respectively) (Table 1).

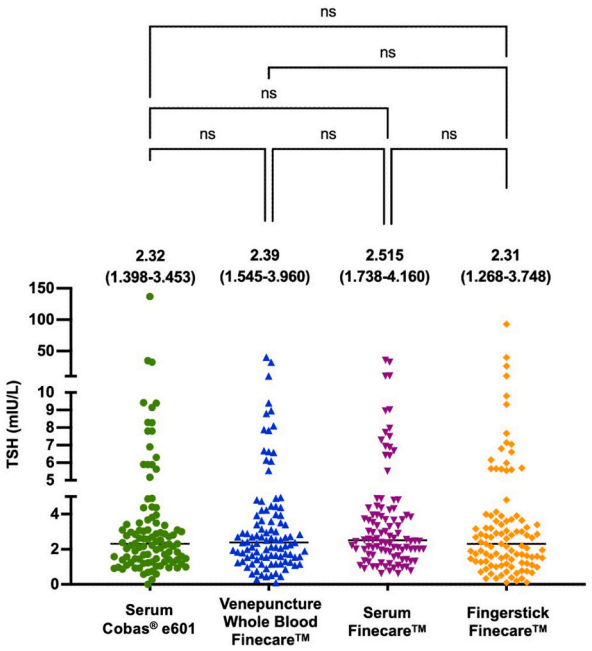

Fig. 1. General distribution of values obtained from fingerstick, venepuncture whole-blood and serum using Finecare™ machine and the reference method, Roche cobas® e 601. The difference between all groups was obtained using the nonparametric Kruskal-Wallis test. The median and the interquartile ranges are presented above each test.
ns, non-significant ($p > 0.05$).

3.2. Sample type (fingerstick, venepuncture whole-blood, or serum) does not significantly affect the results obtained by Finecare™

Finecare™ performance was assessed by comparing the Finecare™ fingerstick, venepuncture, and serum samples to the same serum samples analyzed by Roche cobas® e 601. The general distribution for all numerical values obtained by Finecare™ and the reference method is represented in Fig. 1. There is no significant difference between the overall values and medians obtained by Fincare™ as compared with cobas® e 601 (Fig. 1). These results suggest that sample type has no significant effect on the obtained results (Fig. 1).

3.3. Finecare™ quantitative results are highly correlated with the reference method

We performed a correlation analysis between Roche cobas® e 601 reference method and Finecare™ TSH test values of 102 samples. As indicated in Fig. 2(A-C), both Finecare™ venepuncture whole-blood and fingerstick sample test values have a very strong correlation with Roche cobas® e 601 ($r = 0.95$ and $r = 0.9$ respectively; $p < 0.0001$). Strong correlation was also obtained between Finecare™ serum sample test values and cobas® e 601 ($r = 0.93$, $p < 0.0001$) (Fig. 3A).

Finecare™ venepuncture whole-blood and serum samples showed a strong correlation ($r = 0.95$, $p < 0.0001$) (Fig. 3B). Finecare™ fingerstick showed similar results when compared to the serum sample as in the venepuncture whole-blood samples ($r = 0.85$, $p < 0.0001$) (Fig. 3C). These results confirm that the sampling method (i.e., serum, vs fingerstick vs venepuncture) does not affect the TSH test values, and suggest that Fincare™ can be used for analytical quantitation of TSH regardless of the sampling method.

3.4. Finecare™ showed high true positive and negative rates compared to the reference method

We classified the disease condition according to the test value obtained by the reference method (Table 2). Results are considered positive (diseased) if any of TSH values were below 0.35 or above 4.5 mIU/mL. TSH serum, venepuncture, and fingerstick results were also classified accordingly. As shown in Table 3, the positive and negative values of Finecare™ were comparable to those of the reference method, regardless of the types of samples (with very few exceptions). We believe these exceptions are due to the differences between Finecare and reference method borderline results, which are outside, yet very close, to the upper or lower limit of the normal/reference range (0.35–4.54 mIU/mL).

3.5. Finecare™ has high sensitivity and specificity for diagnosis of thyroid abnormalities

To further confirm our results, a concordance analysis between Finecare™ venepuncture whole-blood and Finecare™ serum was

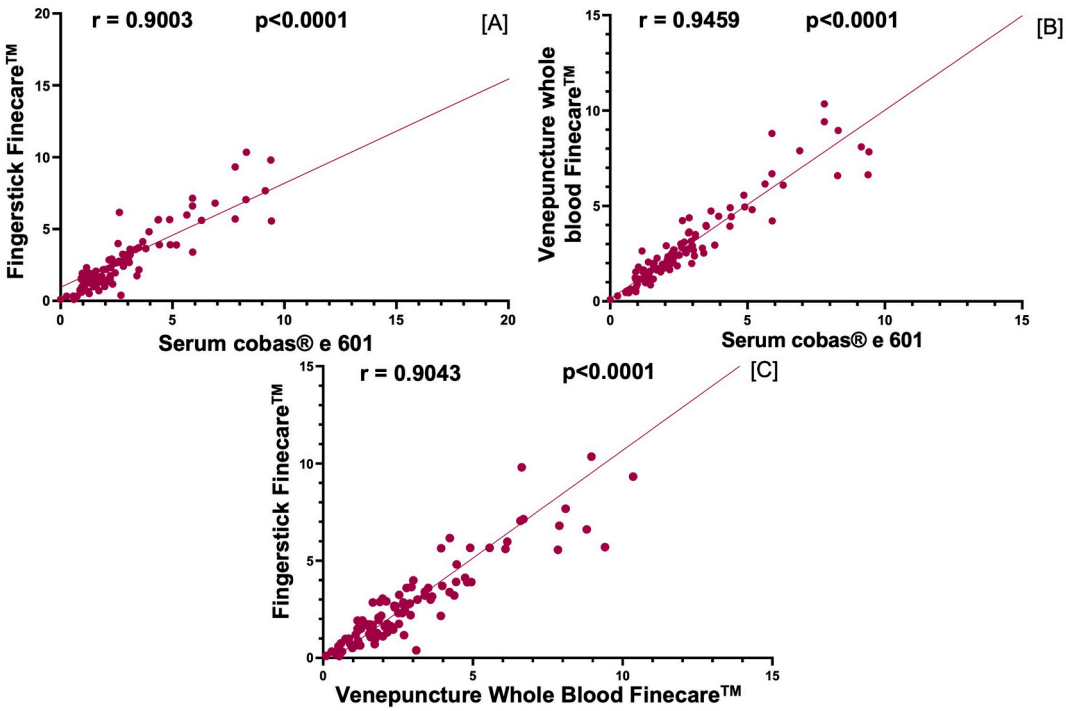

Fig. 2. Pairwise correlation analysis and linear regression analysis of the numerical values obtained by each assay. Spearman correlation coefficient (r) was calculated to be 0.9003, 0.9459, and 0.9043 for [A], [B], and [C], respectively. P values are indicated (<0.0001).

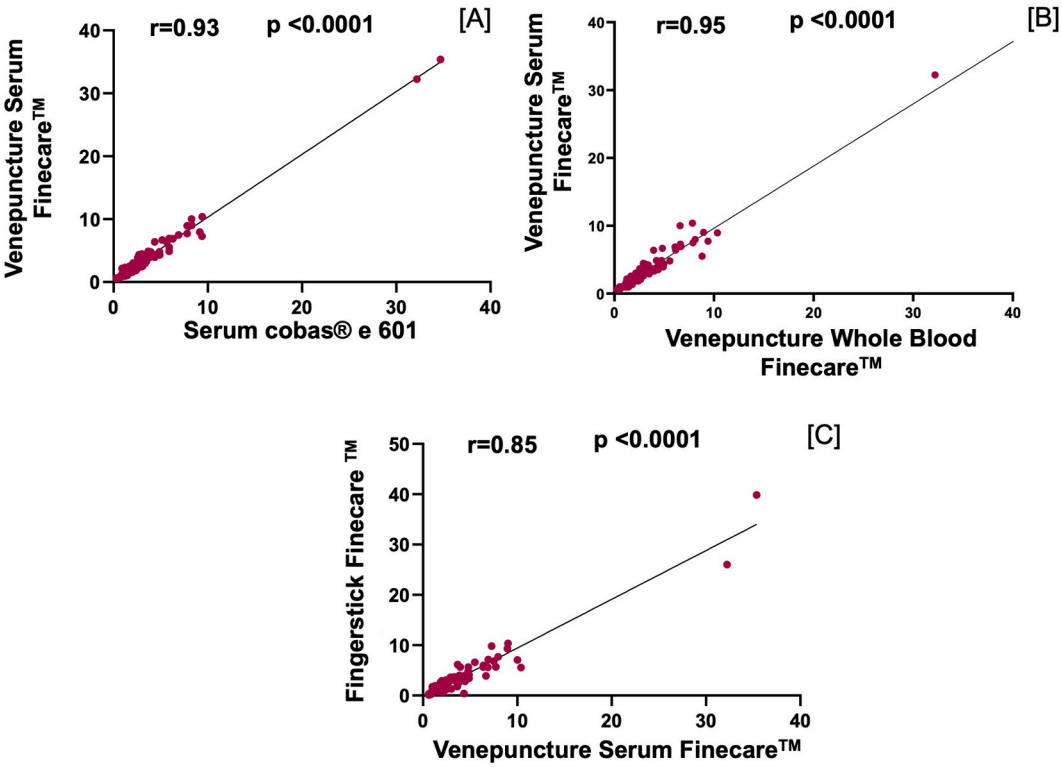

Fig. 3. Pairwise correlation and linear regression analyses of the numerical values obtained by each assay. Spearman correlation coefficient (r) was calculated to be 0.93, 0.95, and 0.85 for [A], [B], and [C], respectively. P values are indicated (<0.0001).

Table 2
A comparison between the three Finecare™ testing methods: venepuncture whole-blood, venepuncture serum, and fingerstick.

A.		Finecare™ Venepuncture Whole-Blood [n = sample]		
		Positive	Negative	Total
Finecare™- Fingerstick	*Positive	19	7	26
	Negative	3	73	76
	Total	22	80	102
Finecare™- Venepuncture Serum	*Positive	19	3	22
	Negative	3	77	80
	Total	22	80	102
B.		Finecare™ Venepuncture-Serum [n = sample]		
Finecare™- Fingerstick	*Positive	19	7	26
	Negative	3	73	76
	Total	22	80	102

*positive value: sample with results outside the reference range.

performed (Table 4). The serum Finecare™ was considered the reference for comparison. The Finecare™ venepuncture whole-blood showed high overall percentage agreement (OPA) of 94.1 % (86.4%–96.3 %), positive predictive value (PPV) of 86.4 % (67.3%–95.1 %), negative predictive value (NPV) of 96.25 % (90%–98.7 %) and an excellent agreement with the Finecare™ serum [Cohen's Kappa = 0.826 (0.692–0.960)]. If Finecare™ serum considered as a reference method, the sensitivity and specificity of Finecare™ venepuncture were 86.4 % (65.1%–97.1 %) and 96.3 % (89.4%–99.2 %), respectively (Table 4). Moreover, Finecare™ venepuncture whole-blood showed high sensitivity and specificity compared to the reference method, 95.2 % and 97.5 %, respectively (Table 4).

Finecare™ serum samples showed a high sensitivity of 95.1 % and a specificity of 90.5 %, yet slightly lower than the venepuncture whole-blood samples when both, serum and venepuncture, were compared to the reference method.

Finecare™ fingerstick also showed good performance but with a lower sensitivity (85.7 %) and specificity (90 %) than the serum and the venepuncture whole blood results (Table 4). When comparing Finecare™ venepuncture whole-blood and serum samples to fingerstick, similar results were obtained with a sensitivity of 90.2 % and specificity of 86.4 % (Table 4). Moreover, different test agreements and Cohen's Kappa statistics were reported between the reference and Finecare™ venepuncture and fingerstick samples.

Table 3
A comparison between the three Finecare™ testing methods (venepuncture whole-blood, venepuncture serum, and fingerstick) against the reference.

		Reference Method: Roche cobas® e 601		
		Positive	Negative	Total
Finecare™- Fingerstick	Positive[a]	18	8	26
	Negative	3	73	76
	Total	21	81	102
Finecare™ Venepuncture- Whole-Blood	Positive[a]	20	2	22
	Negative	1	79	80
	Total	21	81	102
Finecare™ (Venepuncture)- Serum	Positive[a]	19	3	22
	Negative	2	78	80
	Positive	21	81	102

[a] positive value: sample with results outside the reference range.

The OPA, PPV, and NPV between the reference method and venepuncture blood were high: 97.1 %, 90.9 % and 98.8 %, respectively. Comparing Finecare™ fingerstick to the reference method, OPA, PPV, and NPV were lower than those of the venepuncture blood samples; 89.2 %, 69.2 % and 96.1 %, respectively. A good agreement was found between the Finecare™ fingerstick and the reference method (Cohen's Kappa = 0.7) and an almost perfect agreement between the Finecare™ venepuncture and the reference (Cohen's Kappa = 0.91). These results indicate that Fincare™ TSH can be used as a qualitative screening of TSH abnormalities regardless of the source of the specimen withdrawal. This is particularly important in infant and neonatal screening program since it will allow testing with small blood volumes.

3.6. Finecare™ showed a strong correlation with the reference method during a subgroup analysis of abnormal TSH values

A subgroup analysis of low and high TSH values (n = 18) was performed to investigate the correlation of Finecare™ with the cobas® e 601 serum in abnormal samples (Table 5). A strong and significant correlation was reported between cobas® e 601 serum and Finecare™ whole-blood ($r = 0.692$; $p = 0.0015$), and between the reference method and fingerstick test Finecare™ ($r = 0.66$; $p = 0.0025$). A very strong correlation was also observed between cobas® e 601 serum and Finecare™ serum ($r = 0.88$; $p < 0.0001$). Although the correlation results were slightly affected compared to Fig. 3, such analysis should be interpreted with caution because of the small sample size of abnormal TSH values (n = 18) were only included in the analysis.

4. Discussion

Congenital hypothyroidism results from the failure of the thyroid gland to produce adequate levels of the thyroid hormones [27], a condition that requires an immediate diagnosis, especially in newborns. In this regard, the rapid turnaround time, minimal sample volume, and elimination of hematocrit bias make POCT TSH assays the method of choice for newborn thyroid screening [15]. Moreover, POCT TSH assay affordability and ease of use enable thyroid diagnostic testing in resource-limited settings [28].

So far, many POCTs have been developed; however, their performance remains to be compared to standard laboratory approaches. In this study, Finecare™ TSH Rapid Quantitative Test performance was validated along with Finecare™ FIA System for the quantitative determination of TSH in human blood. This test is used as POCT for screening and following up on TSH values in the population. This study employed a total of 102 samples to evaluate the assays' performance. To our knowledge, this is one of the first studies conducted to validate the fluorescence-LFIA-based Finecare™ TSH test, besides the one by Kahaly et al., 2022 where the performance of the Finecare™ TSH test was compared to Abbott [29].

The presented data demonstrate that Finecare™ results are consistent with the reference laboratory method (Roche cobas® e 601) using venepuncture whole-blood, serum and fingerstick samples. Venepuncture whole-blood samples showed excellent sensitivity and specificity, 95.2 % and 97.5 % (Table 3). Excellent agreement between the two tests was also observed (Cohen's Kappa = 0.91) along with a very strong correlation ($r = 0.95$, $p < 0.0001$) (Table 3, Fig. 2). In contrast, Finecare™ serum samples showed slightly less sensitivity and specificity (90.5 % and 96.3 %, respectively) ($r = 0.93$, $p < 0.0001$). This is mainly due to borderline results but not due to significant differences between the values. Since the reference range is set between 0.35 and 4.5 mUI/L, any value outside this range, even with one decimal point, is considered positive, therefore affecting the overall test sensitivity. Although in this study we considered 0.35 and 4.5 mUI/L as the reference range, others laboratories use different ranges (based on the population origin) [21,22,30,31], which is an aspect that results in different sensitivity and specificity values. Nonetheless, correlation results indicate a very strong agreement suggesting that Finecare™ is suitable for quantitative TSH measurement. Furthermore, the Finecare™ fingerstick showed 85.7 % sensitivity and 90 % specificity, fair test agreement (Cohen's Kappa = 0.7) and very strong correlation ($r = 0.9$, $p < 0.0001$). The excellent concordance between the POCT Finecare™ and Roche cobas® e 601 makes it an attractive alternative to the standard laboratory technique in a non-laboratory setting. This has been challenging because almost all of the currently available TSH POCTs were reported to have either high sensitivity but low specificity or vice versa. For instance, TSH-CHECK-1 © (Vedalab, Alençon, France) test sensitivity was 100.0 %, but specificity was 76.6 % [32], indicating high false-positive results, which can possibly be due to cross-reactivity. It is noteworthy to mention that, due to hematocrit variability, it is generally believed that serum or plasma TSH assays are more accurate, affordable, accessible, and clinically useful than tests which measure TSH in a capillary or venepuncture

Table 4
Validity, agreement, and accuracy of Finecare™ in comparison with the reference method.

Reference	Test	OPA (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy/Efficiency (%)	Cohen's Kappa Coefficient
		(CI: 95 %)						
Finecare™ [venepuncture whole-blood]	Finecare™ [serum]	94.1 (86.4–96.3)	86.4 (65.1–97.1)	96.3 (89.4–99.2)	86.4 (67.3–95.1)	96.3 (90–98.7)	94.1 (87.6–97.8)	0.82 (0.69–0.96)
	Finecare™ [fingerstick]	90.2 (86.4–91.3)	86.4 (65.1–97.1)	91.3 (82.8–96.4)	73.1 (56.8–84.9)	96.1 (89.5–98.6)	90.2 (82.7–95.2)	0.73 (0.6–0.89)
Roche cobas® e 601	Finecare™ [venepuncture whole-blood]	97. (95.2–97.5)	95.2 (76.2–99.9)	97.5 (91.4–99.7)	90.9 (71.7–97.5)	98.8 (92.1–99.8)	97.1 (91.6–99.4)	0.91 (0.8–1)
	Finecare™ [serum]	95.1 (90.5–96.3)	90.5 (69.6–98.8)	96.3 (89.6–99.2)	86.4 (67.4–95.1)	97.5 (91.3–99.3)	95.1 (88.9–98.4 %)	0.85 (0.727–0.978)
	Finecare™ [fingerstick]	89.2 (85.7–90.1)	85.7 (63.7–97)	90 (81.5–96)	69.2 (53.2–81.6)	96.1 (89.5–98.6)	89.2 (81.5–94.5)	0.7 (0.53–0.9)
Finecare™ [serum]	Finecare™ [fingerstick]	90.2 (86.4–91.3)	86.4 (65.1–97.1)	91.3 (82.8–96.4)	73.1 (56.8–84.9)	96.1 (89.5–98.6)	90.2 (82.7–95.2)	0.73 (0.6–0.89)

OPA, overall percentage agreement; PPV, positive predictive value; NPV, negative predictive value.

Table 5
Correlation of abnormal TSH values on cobas® e 601 serum and Finecare™ (serum, whole-blood, and fingerstick).

Comparison of Study Groups	Spearman correlation (r)	p-value
Venepuncture test cobas® e 601 serum and venepuncture test Finecare™ whole-blood	0.692	0.0015
Venepuncture test cobas® e 601 serum and venepuncture test Finecare™ serum	0.88	<0.0001
Venepuncture test cobas® e 601 serum and fingerstick test Finecare™	0.66	0.0025

whole-blood sample [33].

There are great advantages to using Finecare™ as POCT since results can be obtained in a short period of time, and there is no need for lengthy sample processing since capillary blood can be used (easy to collect with small volumes), especially for neonates. Fingerstick samples analyzed by Finecare™ showed a very strong correlation with the reference method ($r = 0.9$), making it feasible for TSH screening and following up on quantitative measurement.

There are a few variations between the data obtained with Finecare™ fingerstick and the reference method. Such variations are primarily due to technical errors rather than instrumental faults, which could be attributed to incorrect fingerstick sampling or sample clotting at the time of sample collection. As a result, sample clotting could occur. Our results were also limited with the use of one anticoagulant (EDTA) as recommended by the manufacturer. The collection tube of Wondfo TSH kit does not have heparin; thus, partial clotting in the sample could affect the results. Future studies should focus on testing blood collected in the heparinized capillary tube. Moreover, anticoagulants for fingerstick samples were not used, which could have contributed to minor discrepancies between Finecare™ and the reference method. Additionally, other issues could derive from mistakes or inaccuracies in volume pipetting when withdrawing the fingerstick samples since the test requires the handling of relatively large volumes from the tip of the finger (75 μL). Variations in fingerstick and cobas® e 601 results could also happen due to artifact from skin contaminants during sample withdrawal. Finally, variations between assays are expected since the used test principles are different. In this regard, studies had reported variabilities in values also when similar test principles such as CLIA and ELISA were used [34]. Discrepancies in values obtained by Roche Cobas and Abbott TSH test were reported [35], although both companies are considered leading CLIA manufacturers worldwide. Future investigations should also focus on evaluating and comparing Finecare™ to reference methods other than Roche cobas® e 601 such as Abbott, DiaSorin and Vitros System.

5. Conclusion

This study aimed to evaluate the performance of the Finecare™ TSH Rapid Quantitative Test for the measurement of TSH using fingerstick, venepuncture whole-blood, and serum samples. The main objective was to assess the accuracy, sensitivity, and specificity of Finecare™ compared to the reference method, Roche cobas® e 601, and determine the suitability of Finecare™ as a point-of-care testing option for TSH measurement. The results of this study demonstrated that Finecare™ exhibited high sensitivity, specificity, and overall agreement for measuring TSH levels in comparison to the reference method. A strong degree of correlation was also portrayed between Finecare™ and cobas® e 601, indicating its reliability and accuracy. Importantly, this study revealed that sample type (fingerstick, venepuncture whole-blood, or serum) did not significantly affect the results obtained by Finecare™.

Based on these findings, Finecare™ can be considered a reliable assay for screening and monitoring TSH values in the population, particularly in non-laboratory or small laboratory settings. However, to further enhance its usability, it is recommended that the company reduces the sample volume required and considers implementing the use of heparinized tubes for blood withdrawal, which could improve accuracy and minimize clotting issues.

In summary, our study provides evidence that Finecare™ is a valuable tool for TSH measurement in a point-of-care setting. Its high sensitivity, specificity, and correlation with the reference method support its reliability and effectiveness. By facilitating rapid and accessible TSH testing, Finecare™ has the potential to improve thyroid disease screening and management, enhancing patient care in diverse healthcare settings.

Ethics statement

Our study complies with all ethical regulations of the Office of Academic Research-Qatar University Institutional Review Board (QU-IRB), and granted the ethical number: QU-IRB 1766-E/22.

Authors contribution

SS and FT: Data analysis and interpretation, wrote the first draft of the manuscript; MMA: Contributed reagents and materials, performed the experiments. DE: wrote the first draft of the manuscript; edited and reviewed the final version of the manuscript: SY: Data analysis and interpretation, critically edited the final version of the manuscript: AFM: Study design, critically reviewed the final version of the manuscript. GP: Study design, critically reviewed the final version of the manuscript. ND: Study design, critically reviewed the final version of the manuscript. GKN: Conceived and designed the whole study, data acquisition, and critically reviewed the final version of the manuscript.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Mahmoud M. Al Ghwairi reports equipment, drugs, or supplies was provided by Guangzhou Wondfo Biotech Co Ltd. Gheyath K. Nasrallah reports article publishing charges was provided by Heliyon.

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