Practical Laboratory Medicine 42 (2024) e00432

Contents lists available at ScienceDirect

Practical Laboratory Medicine

journal homepage: www.elsevier.com/locate/plabm

Registered Report Stage II

Performance evaluation of $Eu3^{+}$-based CRP/SAA and PCT/IL-6 lateral flow immunoassay kits and their diagnostic value in respiratory tract infections

Mingxin Lin [a,1], Jing Zhang [a,1], Jianxing Cai [a,1], Jumei Liu [a], Min Zhu [a], Ke Li [b], Miaoyun Hu [c], Chenxi Li [a,**], Huiming Ye [a,*]

[a] Department of Laboratory Medicine, Fujian Key Clinical Specialty of Laboratory Medicine, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, China
[b] Department of Laboratory Medicine, Xiamen Medical College, Xiamen, China
[c] Department of Laboratory Medicine, Xiamen Huaxia College, Xiamen, China

ARTICLE INFO

Keywords:
Detection performance
Diagnostic performance
Respiratory tract infections
Lateral flow immunoassay

ABSTRACT

Objectives: Respiratory infections are among the most common infectious diseases, resulting in significant morbidity and mortality. C-reactive protein (CRP), serum amyloid A (SAA), procalcitonin (PCT), and interleukin-6 (IL-6) are advantageous for diagnosing respiratory tract infections. This study assessed the analytical performance and accuracy of new kits for $Eu3^{+}$-based CRP/SAA and PCT/IL-6 lateral flow immunoassay and its diagnostic value in respiratory tract infections.

Methods: This study evaluated the detection performance of a test kit using guidelines from the Center for Medical Device Evaluation (CMDE) and the Clinical and Laboratory Standards Institute (CLSI). The test results were compared to those of the commercial kits (CRP: Mindray; SAA: Norman; PCT: Shanghai Upper; IL-6: Wantai BioPharm). A total of 156 patients with respiratory tract infections (53 with bacterial infections (Bac group); 50 with viral infections (Vir group); and 53 with co-infections (Bac + Vir group)) were enrolled, along with 50 healthy controls (HC group). Venous blood samples were collected to measure levels of SAA, PCT, CRP, and IL-6 using both the test and commercial kits. The diagnostic value of these biomarkers was assessed using receiver operating characteristic (ROC) curves.

Results: Correlation analysis demonstrated a strong concordance between the test kits and commercial kits (CRP: $r = 0.9396$, $P < 0.0001$; SAA: $r = 0.8986$, $P < 0.0001$; PCT: $r = 0.9594$, $P < 0.0001$; IL-6: $r = 0.9009$, $P < 0.0001$). The diagnostic performance of the test kits in identifying bacterial, viral, and co-infections was highly consistent with that of the commercial kit.

Conclusions: The $Eu3^{+}$-based CRP/SAA and PCT/IL-6 lateral flow immunoassay test kits demonstrated high levels of consistency with commercial kits in terms of quantitative outcomes and diagnostic performance for respiratory tract infections.

* Corresponding author. Department of Clinical Laboratory, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, 361003, China.
** Corresponding author. Department of Clinical Laboratory, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, 361003, China.
E-mail addresses: lichexi_09@126.com (C. Li), yehuiming@xmu.edu.cn (H. Ye).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.plabm.2024.e00432
Received 23 June 2024; Received in revised form 23 September 2024; Accepted 26 September 2024
Available online 27 September 2024

1. Introduction

Respiratory infections are among the most common infectious diseases, resulting in high morbidity and mortality, especially in immunocompromised patients. Millions of people worldwide die from respiratory infections each year, making them one of the six leading causes of death across low-, middle-, and high-income countries. These infections impose a significant economic burden on healthcare services globally. Respiratory infections can occur in various community and hospital settings, affecting both adults and children, and can present with a wide range of clinical symptoms, from minimal to severe outbreaks [1,2]. Respiratory tract infections are often caused by diverse pathogens and lack typical clinical symptoms, complicating early diagnosis. Studies indicate that more than 50 % individuals with respiratory tract infections receive antibiotic treatment, yet there is widespread misuse of antibiotics, especially in non-bacterial infections [3]. Therefore, identifying the specific pathogen responsible for the infection is crucial for determining appropriate treatment. Isolating and culturing pathogens from respiratory tract infections is both difficult and time-consuming. Serum markers are simple, rapid, and have certain diagnostic value. Serum markers, such as serum amyloid A (SAA), C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6), offer a simple and rapid diagnostic approach with significant value. These markers are effective in identifying infectious pathogens, improving diagnostic accuracy, and reducing antibiotic misuse [4,5]. However, in resource-limited or emergency situations, the rapid and sensitive detection of these markers without the need for sophisticated equipment or technical personnel is essential for point-of-care diagnosis of severe diseases.

Lateral flow immunoassay (LFIA) is a classic point-of-care testing (POCT) technique that offers rapid detection, characterized by simplicity, speed (results in 5–15 min), low sample volume requirements, and no need for specialized equipment [6]. Lanthanide elements, with their narrow emission spectra and long fluorescence lifetimes, are advantageous in such assays. By delaying the measurement time for each excitation light pulse and recording the specific fluorescence emitted by long-lived lanthanide chelates after the background fluorescence has decayed, we can avoid interference and improve detection accuracy [7]. Therefore, the combination of lateral flow immunoassay (LFIA) and lanthanide elements is widely used in the biomedical field. In this study, we aimed to evaluate the performance of $Eu3^{+}$-based CRP/SAA and PCT/IL-6 lateral flow immunoassay kits and explore their diagnostic value in pediatric respiratory tract infections.

2. Materials and methods

2.1. Assays

$Eu3^{+}$-based CRP/SAA and PCT/IL-6 lateral flow immunoassay kits were developed by Wantai Biological Pharmacy Enterprise (Beijing), which served as the testing kit. These reagents employ a double-antibody sandwich detection approach. The CRP/SAA and PCT/IL-6 were detected using two mouse monoclonal antibodies. When CRP, SAA, PCT, or IL-6 is present in the sample, it binds with the Eu3+-Ab1 probes, and the immune complex is captured by the Ab2 coated on the T line via immunoreaction. This forms a “Eu3+-Ab1-CRP/SAA or PCT/IL-6-Ab2” sandwich, resulting in a fluorescent band on the T line. Excess probes migrate on the NC membrane and bind with the goat anti-mouse IgG coated on the C line, forming another fluorescent band. When CRP, SAA, IL-6, or PCT is absent in the sample, only a visible fluorescent band appears on the C line. The qualitative result can be observed under ultraviolet light, with a positive result indicated by two fluorescent lines on the T and C lines, and a negative result by a single fluorescent band on the C line. For quantitative detection, the fluorescent intensity of the T (FIt) and C lines (FIc) are obtained and recorded by a portable reader. The ratio between FIt and FIc (T/C) is calculated, effectively offsetting the effects of the inherent heterogeneity of test strips and the sample matrix. T/C is proportional to the CRP, SAA, PCT, or IL-6 level in the sample. "The commercial kit served as the comparative kit. CRP detection was performed using the Mindray BC-5390 instrument with original reagents. The Norman NRM411-S7 specific protein analyzer with original reagents was used to detect SAA levels, the Shanghai Upper OTTOMAN-1000 with original reagents for PCT levels, and the Wantai CARIS 200 with original reagents for IL-6 levels. All operations were carried out according to the kit and instrument instructions.

2.2. Calibration curve

Calibration curves were generated using a range of calibration solution concentrations: 0.2, 1.4, 2, 10, 50, 100, and 200 mg/L for CRP; 7, 10, 50, 250, 500, and 1000 mg/L for SAA; 0.05, 0.2, 0.5, 2, 10, 20, and 50 ng/mL for PCT; and 50, 200, 1000, 2500, and 5000 pg/mL for IL-6. A four-parameter logistic curve was used for fitting the calibration data. All calibration solution concentrations are traceable to certified reference materials or standards. The CRP calibration solution concentrations were based on the WHO International Standard (NIBSC code: 85/506); SAA calibration solution concentrations followed the WHO International Standard (NIBSC code: 92/680); IL-6 calibration solution concentrations were determined using an enterprise calibrator traceable to the WHO International Standard (NIBSC code: 89/548); and PCT calibration solution concentrations were determined using an enterprise calibrator traceable to the Roche system.

2.3. Limit of detection

A zero-concentration sample was used as the detection sample. The measurement was repeated 20 times, and the mean (M), standard deviation (SD), and M $\pm$ 2SD were calculated.

2.4. Linear range

A series of evaluation samples were prepared by selecting different concentrations of plasma samples. Each sample was measured three times, and the average was calculated. In standard regression analysis, T/C and matching concentrations were used as the y and x variables, respectively, to evaluate the linear range.

2.5. Accuracy

We have verified the accuracy using calibration products for CRP, SAA, and IL-6 at high, medium, and low concentrations provided by Wantai Biopharma. For each concentration level, we performed three repeated measurements to ensure accuracy. Due to the lack of an international reference standard for PCT, we verified its accuracy through a recovery test. We prepared 50 ng/mL PCT calibration solutions and a matrix serum sample. Subsequently, 50 μL of the PCT calibration solution was added to 950 μL of the matrix serum sample to obtain the mixed sample. Each sample was tested three times, and their respective means were calculated. Recovery rates between 85 % and 115 % were considered acceptable.

2.6. Precision

The precision of the detection kit was evaluated based on inter-day and intra-day measurements using high-level and low-level samples. For intra-day analysis, the samples were measured 20 times each day. In the inter-day study, the samples were analyzed over three consecutive days, with each measurement repeated five times daily.

2.7. Study population

A total of 156 patients diagnosed with respiratory tract infections in our hospital from March 2023 to September 2024 were selected as the study subjects. All patients underwent chest radiography, bacterial culture using blood, sputum, nasopharyngeal swab, pleural fluid, or breast aspiration samples, and multiplex PCR for nucleic acid detection. Patients were categorized into the bacterial infection group (Bac group), viral infection group (Vir group), co-infection group (Bac + Vir group), and healthy control group (HC group). The Bac group (n = 53) were included were included as follow: 1) radiographic signs suggestive of bacterial lower respiratory tract infection (such as pleural effusion, consolidation, lobar involvement); 2) Positive bacterial culture from blood, sputum, nasopharyngeal swab, pleural fluid, or transthoracic aspiration samples.; 3) negative viral test results. The Vir group (n = 50) were included in the following criteria: 1) normal chest X-ray or patterns indicative of viral lower respiratory tract infection (interstitial infiltrates and peribronchial infiltrates); 2) negative bacterial cultures; 3) positive viral test results. The Bac + Vir group (n = 53) comprised the symptoms of mixed infection. Healthy children (n = 50) were included based on the following criteria: 1) normal laboratory indicator levels; 2) no symptoms of infection. This study was approved by the Ethics Committee of Women and Children's Hospital, Xiamen University (Number: KY-2023-074-H01).

2.8. Method comparison

Methods from different manufacturers were compared. The levels of CRP, SAA, PCT, and IL-6 in children with respiratory tract

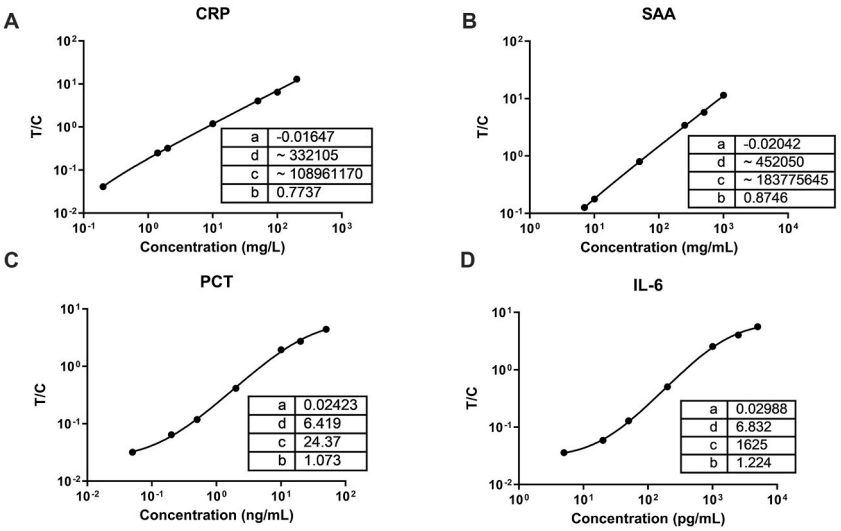

Fig. 1. Calibration curve of analytes. (A) CRP, (B) SAA, (C) PCT, (D) IL-6.

infections were evaluated simultaneously using both the test and commercial kits to analyze the correlation between the two kits.

2.9. Statistical analysis

Statistical software SPSS (version 22.0) and GraphPad Prism 7 were used to manage and analyze the data. A p-value of <0.05 was considered statistically significant. Continuous quantitative data were described using the mean ± standard deviation (SD), and the independent sample *t*-test was used for comparing continuous variables between patients and healthy controls. The Pearson contingency coefficient was used to determine the correlation between the test and commercial kits, and an equation was generated by simple linear regression analysis. Receiver operating characteristic (ROC) curves were constructed to calculate the area under the curve (AUC) to assess the diagnostic effectiveness for respiratory tract infections.

3. Results

3.1. Calibration curve of $Eu3^+$-based CRP/SAA and PCT/IL-6 FLA kits

Calibration curves of the analytes are shown in Fig. 1. Typical regression equations.

Were derived as Y(CRP)=((−0.01647-324699)/(X-324699)-1)ˆ(1/0.7737)*1.058*10ˆ8(R square = 0.9975),Y(SAA)=((−0.02042-345522)/(X-345522)-1)ˆ(1/0.8746)*1.352*10ˆ8 (R square = 0.9986), Y(PCT)= ((0.02423–6.419)/(X-6.419)-1)ˆ(1/1.073)*24.37(R square = 0.9964) and Y(IL-6)= ((0.02988–6.832)/(X-6.832)-1)ˆ(1/1.224)*1625 (R square = 0.9978).

3.2. Limit of detection of $Eu3^+$-based CRP/SAA and IL-6/PCT FLA kits

Twenty replicates of zero-concentration samples were used to determine the limit of the blank. The limits of the blank were 0.05 mg/mL for CRP, 1.00 mg/L for SAA, 0.04 ng/L for PCT, 2.24 pg/mL for IL-6 (Table 1).

3.3. Linear range of $Eu3^+$-based CRP/SAA and PCT/IL-6 FLA kits

Samples with different concentration levels were used to validate the linear range of the test kit. These results are presented in Fig. 2. The typical regression equations of CRP, SAA, PCT and IL-6 were Y = 1.0612X+0.6558 (R^2 = 0.9998), Y = 0.9497X+8.202 (R2 = 0.9993), Y = 0.9872X+0.0831 (R2 = 0.9997) and Y = 0.999X+7.4454 (R2 = 0.994), respectively. The linear range of CRP, SAA, PCT and IL-6 was 0.2–200 mg/L, 7–1000 mg/L, 0.05–50 ng/mL, and 5–5000 pg/mL, respectively.

3.4. Accuracy and precision of $Eu3^+$-based CRP/SAA and PCT/IL-6 FLA kits

The accuracy of CRP, SAA and IL-6 was tested by enterprise reference products, and the results were no more than ±15 % (Table 2). The accuracy of the PCT was evaluated using a recovery test. The mean recovery percentages were 91.00 % (Table 3). These findings indicated the acceptable accuracy of the kits. The precision results are summarized in Table 4. The CV of intra- and inter-assay precision of CRP was 9.59 %–12.55 % and 8.57 %–13.59 % respectively. The CV of the intra- and inter-assay precision of SAA was 7.81 %–14.41 % and 6.89 %–11.33 %, respectively. The CV of the intra- and inter-assay precision of PCT was 9.80 %–14.61 % and 13.40 %–16.13 %, respectively. The CV of the intra- and inter-assay precision of IL-6 was 12.30 %–12.75 % and 12.55 %–14.15 %, respectively.

3.5. Method comparison between commercial kits and test kits

To compare the two methods, 156 blood and serum samples were analyzed using the test kits and commercial kits. Satisfactory relevance and consistency were observed (Fig. 3). The correlation study with the test kits and commercial kits demonstrated similarity between the two methods (CRP: r = 0.9396, P < 0.0001; SAA: r = 0.8986, P < 0.0001; PCT: r = 0.9594, P < 0.0001, PCT: r = 0.9009, P < 0.0001). The regression equations of the logarithmically transformed results of the two methods were Y = 1.533X+4.514 (R^2 = 0.8828, P < 0.0001) for CRP, Y = 1.577X+14.340 (R2 = 0.8074, P < 0.0001) for SAA, Y = 1.747X+0.644 (R2 = 0.9205, P < 0.0001) for PCT, and Y = 0.8754X+3.910 (R2 = 0.8116, P < 0.0001) for IL-6.

Table 1
The limit of blank.

	Mean of T/C	SD	LOB
CRP(mg/L)	0.01	0.02	0.05
SAA(mg/L)	1.00	0.00	1.00
PCT(ng/ml)	0.02	0.01	0.04
IL-6(pg/ml)	1.03	0.60	2.24

SD, standard deviation; LOB, limit of blank.

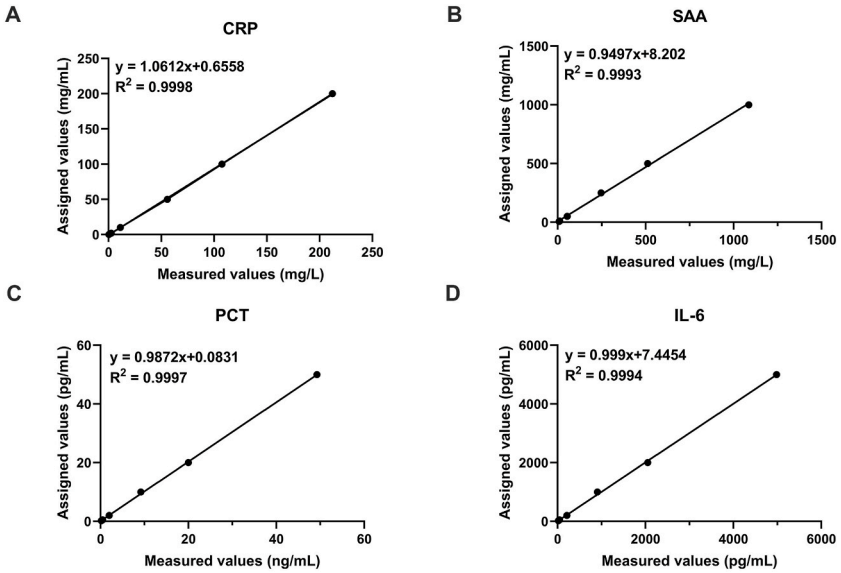

Fig. 2. The linear range of the test kit. (A) CRP, (B) SAA, (C) PCT, (D) IL-6.

Table 2
The accuracy of CRP, SAA and IL-6.

		Assigned values	Times			Measured value	Bias (%)
			1	2	3		
CRP (mg/L)	Low level	10.00	10.50	10.50	10.70	10.57	5.67
	Medium level	50.00	52.80	52.30	52.50	52.53	5.07
	High level	150.00	160.90	159.01	161.70	160.54	7.02
SAA (mg/L)	Low level	10.00	9.00	11.00	11.00	10.33	3.33
	Medium level	250.00	260.00	257.00	260.00	259.00	3.60
	High level	500.00	562.00	548.00	553.00	554.33	10.87
IL-6 (pg/mL)	Low level	6.00	7.00	7.00	6.00	6.67	7.22
	Medium level	500.00	525.00	519.00	528.00	524.00	11.11
	High level	1000.00	1100.00	1109.00	1106.00	1105.00	10.05

Table 3
The Recovery rate of PCT.

	1	2	3	mean	Recovery rate
C (ng/ml)	0.174	0.19	0.175	0.179	91 %
C (ng/ml)	2.442	2.712	2.4	2.442	
V_0 (ul)	950	950	950	950	
V (ul)	50	50	50	50	
C_s (ng/ml)	50	50	50	50	

V: volume of the PCT calibration solution; V_0: volume of the matrix serum sample; *c*: measured concentration mean of the mixed sample; c_0: measured concentration mean of the matrix serum sample; c_s: concentration of the PCT calibration solution.

3.6. Diagnostic Values of Biomarkers in patient with bacterial, viral, or Co-infections in respiratory tract infection between commercial kits and test kits

ROC curve analysis was used for the assessment of the diagnostic values of SAA, PCT, IL-6, and CRP in patient with bacterial, viral, or co-infections in respiratory tract infection between commercial kits and test kits. As illustrated in Fig. 4, the AUCs of CRP from test kit in HC vs. Bac, HC vs. Vir, HC vs. Bac + Vir, Bac vs. Vir, Bac vs. Bac + Vir and Vir vs. Bac + Vir were 0.991, 0.896,1, 0.832, 0.682, and 0.933, respectively. The results were similar to those of the commercial kit, in which the AUCs of CRP were 0.988, 0.841, 0.999, 0.822, 0.687, and 0.930, respectively. The AUCs of SAA from test kit in HC vs. Bac, HC vs. Vir, HC vs. Bac + Vir, Bac vs. Vir, Bac vs. Bac + Vir and Vir vs. Bac + Vir were 0.796, 0.743, 0.961,0.599, 0.726, and 0.819, respectively. The results were similar to those of the commercial kit, in which the AUCs of SAA were 0.873, 0.733, 0.968, 0.651, 0.747, and 0.839 respectively. The AUCs of PCT from test kit in

Table 4
Evaluation of Intra-assay and Inter-assay precision.

		Intra-assay					Inter-assay				
		Min	Max	Mean	SD	CV(%)	Min	Max	Mean	SD	CV(%)
CRP (mg/L)	Low level	1.80	2.80	2.39	0.30	12.55	2.80	4.60	3.68	0.50	13.59
	High level	81.20	114.00	93.55	8.97	9.59	38.5	52.20	46.70	4.00	8.57
SAA (mg/L)	Low level	9.00	13.00	11.10	1.60	14.41	23.00	34.00	27.80	3.15	11.33
	High level	410.00	521.00	445.60	34.79	7.81	299.00	396.00	342.35	23.59	6.89
PCT (ng/mL)	Low level	0.44	0.59	0.51	0.05	9.80	0.23	0.39	0.31	0.05	16.13
	High level	9.38	14.23	11.84	1.73	14.61	3.43	3.52	2.91	0.39	13.40
IL-6 (pg/mL)	Low level	37.00	56.00	46.00	5.66	12.30	35.00	51.00	44.45	5.58	12.55
	High level	797.00	1174,00	1004.00	128.01	12.75	581.00	765.00	671.00	94.95	14.15

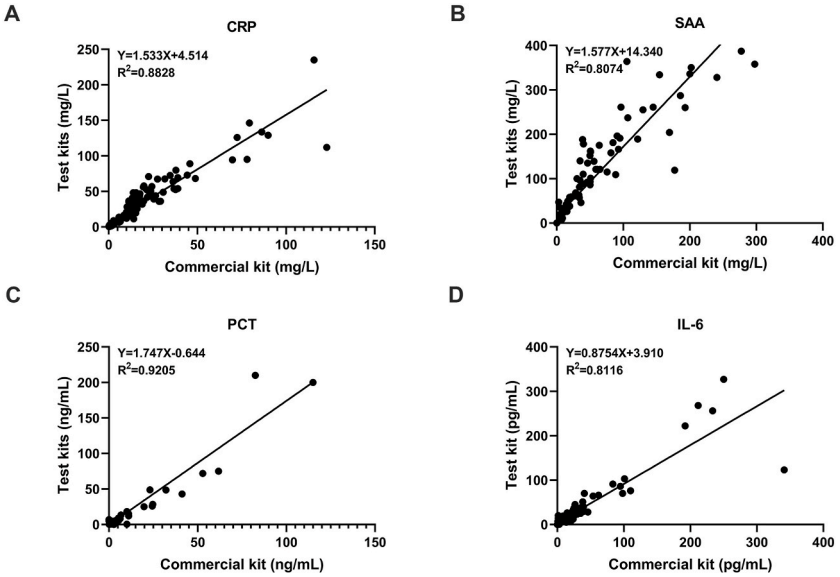

Fig. 3. Method comparisons (A) CRP (B) SAA (C) PCT (D) IL-6.

HC vs. Bac, HC vs. Vir, HC vs. Bac + Vir, Bac vs. Vir, Bac vs. Bac + Vir and Vir vs. Bac + Vir were 0.781, 0.607, 0.863, 0.687, 0.458, and 0.751, respectively. The AUCs of PCT in the commercial kit were 0.838, 0.805, 0.950, 0.688, 0.445, and 0.759 respectively. The AUCs of IL-6 from test kit in HC vs. Bac, HC vs. Vir, HC vs. Bac + Vir, Bac vs. Vir, Bac vs. Bac + Vir and Vir vs. Bac + Vir were 0.800, 0.784, 0.881, 0.572, 0.570, and 0.673, respectively. The AUCs of IL-6 in the commercial kit were 0.821,0.824, 0.831,0.562, 0.518, and 0.594respectively. Our findings showed that the diagnostic performance of the test kit is consistent with that of commercial kit.

4. Discussion

Bacterial, viral, and co-infections often lead to severe respiratory diseases, and even sepsis [8–11]. Therefore, effective biomarkers that can distinguish infection states are crucial for providing targeted treatments for these conditions. Currently, many acute-phase proteins or cytokines are widely used in the clinical diagnosis of infections, such as CRP, SAA, PCT, and IL-6 [12–14]. However, in resource-limited or emergency situations, it is urgent and necessary to rapidly and sensitively detect these biomarkers without the need for large specialized equipment or technical personnel for the immediate diagnosis of serious diseases.

In this study, the performance of new kits for Eu3+-based CRP/SAA and PCT/IL-6 Lateral flow immunoassay from Wantai Bio-Pharm (Beijing) was evaluated, including calibration curve, limit of detection, linear range, accuracy, precision. The results of the test kits were compared to those of commercial kits. More importantly, the test kits demonstrated high consistency with the commercial kits in terms of quantitative results. We further explored the diagnostic value of SAA, CRP, IL-6, and PCT in differentiating various types of infections using both the test kits and commercial kits. Results from both kits showed that CRP, SAA, PCT, and IL-6 have high sensitivity and specificity in distinguishing healthy individuals from those with viral, bacterial, or co-infections. In terms of diagnostic value for viral versus bacterial infections, CRP had the largest AUC area compared to IL-6 and SAA, suggesting that CRP is a superior biomarker for distinguishing between bacterial and viral infections. For differentiating co-infections from bacterial infections, we found that CRP and SAA had higher sensitivity, and specificity than PCT and IL-6, indicating that combined analysis of SAA and CRP can help distinguish bacterial infections from co-infections. Additionally, in distinguishing co-infections from viral infections, CRP and

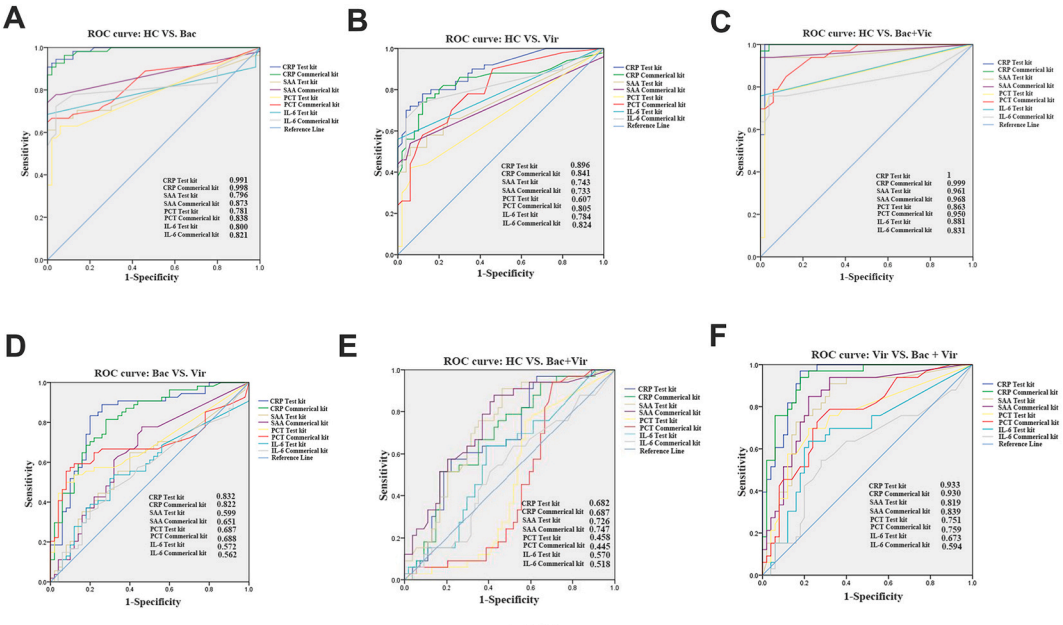

Fig. 4. Diagnostic Values of Biomarkers in patient with Bacterial, Viral, or Co-Infections in respiratory tract infection between commercial kits and test kits (A) ROC curves for SAA, PCT, IL-6, and CRP for discrimination between bacterial infection and healthy control (B) ROC curves for SAA, PCT, IL-6, and CRP for discrimination between Viral infection and healthy control (C) ROC curves for SAA, PCT, IL-6, and CRP for discrimination between co-infection and healthy control. (D) ROC curves for SAA, PCT, IL-6, and CRP for discrimination between bacterial and Viral infection (E) ROC curves for SAA, PCT, IL-6, and CRP for discrimination between bacterial infection and co-infection (F) ROC curves for SAA, PCT, IL-6, and CRP for discrimination between Viral infection and co-infection.

SAA again showed higher sensitivity, and specificity compared to PCT and IL-6, suggesting that combined analysis of SAA and CRP is useful in differentiating co-infections from viral infections. Due to the complexity of respiratory infections, no single biomarker can adequately differentiate between viral, bacterial, or co-infections. Instead, a combination of these biomarkers is essential for accurate disease diagnosis [15]. The method, which can detect two biomarkers using a single test strip, is not only efficient but also simple to operate and cost-effective. This approach is potentially useful in both laboratory and clinical settings. Therefore, utilizing these test kits facilitates point-of-care testing (POCT) for some severe diseases, enabling immediate detection and intervention.

The new test kits offer significant advantages in primary healthcare settings, not only improving accessibility and convenience but also greatly reducing patient wait times, enhancing overall medical efficiency and workflow, and ultimately achieving cost-effectiveness. Firstly, the compact structure and simple design of these testing devices make them easy to operate and suitable for various environments, including community health centers, mobile clinics, and home visits. This feature allows the test kits to be widely used in primary healthcare institutions, especially in resource-limited or underdeveloped areas. In these places, medical resources are often scarce, and traditional testing equipment tends to be bulky and complex, with high usage thresholds, hindering widespread adoption and promotion. Secondly, these test kits can quickly screen and monitor severe infectious diseases. In the field of public health, particularly during outbreaks or emergencies, rapid and accurate disease detection is crucial. By facilitating large-scale testing and immediate intervention measures, they can effectively control the spread of epidemics, alleviate public health pressure, and protect more people's health and lives. Additionally, these portable test kits have significant advantages in reducing medical costs. Traditional laboratory testing equipment is not only expensive but also costly to maintain, while these new test kits are relatively affordable and easy to use, reducing the financial burden on both medical institutions and patients. Moreover, the widespread use of these test kits can significantly improve the efficiency and quality of medical services. Doctors and healthcare workers can obtain test results more quickly, allowing them to timely formulate and adjust treatment plans, thus improving patient outcomes and experiences. Meanwhile, optimized workflows help medical institutions manage resources more effectively, enhancing service capacity and response speed. In summary, the promotion of these new test kits in primary healthcare institutions has led to significant improvements in accessibility, convenience, and cost-effectiveness. They have also played an important role in enhancing medical efficiency and workflow and in improving public health initiatives. Particularly in the face of outbreaks or emergencies, the rapid detection capability and convenience of these test kits provide strong support for public health prevention and control efforts.

There are some limitations in our study that need to be addressed. The small sample size is the primary limitation of this research. These preliminary data must be validated with a larger sample size to determine their effectiveness. Furthermore, due to the limitations of our laboratory conditions, we only selected reagents from a few publicly listed companies for methodological comparison, without comparing them to standard methods. In the future, we plan to collaborate with multiple centers to compare these immunoassay kits with the standard measurement methods and to expand the sample size for further validation.

In summary, we conducted a transparent comparison between the $Eu3^{+}$-based CRP/SAA and PCT/IL-6 lateral flow immunoassay kits developed by Wantai Biological Pharmacy Enterprise and commercial kits. Two methods were performed on the same samples. The test kits were highly consistent with the commercial kits in terms of quantitative results and the diagnosis of respiratory tract infections.

5. Ethics statement

This study was approved by the Ethics Committee of Women and Children's Hospital, Xiamen University (Number: KY-2023-074-H01). All patients provided signed informed consent.

Funding

This work was sponsored by Major Science and Technology Project of Fujian Provincial Health Commission (2021ZD01006), Fujian Provincial Health Technology Project (2020QNB069), Medical and Health Guidance Project of Xiamen (3502Z20214ZD1227).

CRediT authorship contribution statement

Mingxin Lin: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Investigation, Formal analysis, Data curation. **Jing Zhang:** Writing – original draft, Methodology, Investigation, Data curation. **Jianxing Cai:** Software, Investigation, Formal analysis. **Jumei Liu:** Software, Investigation, Data curation. **Min Zhu:** Writing – review & editing, Writing – original draft, Software. **Ke Li:** Writing – review & editing, Writing – original draft. **Miaoyun Hu:** Writing – review & editing, Writing – original draft. **Chenxi Li:** Supervision, Project administration, Funding acquisition, Conceptualization. **Huiming Ye:** Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.plabm.2024.e00432.

References

[1] A. Zumla, Current trends and newer concepts on diagnosis, management and prevention of respiratory tract infections, Current opinion in pulmonary medicine 19 (3) (2013) 189–191.
[2] F. Blasi, A. Torres, Respiratory infections management: still a challenge, Pulm. Pharmacol. Therapeut. 32 (2015) 117–118.
[3] G.B. Rattinger, C.D. Mullins, I.H. Zuckerman, E. Onukwugha, L.D. Walker, A. Gundlapalli, M. Samore, S. Delisle, A sustainable strategy to prevent misuse of antibiotics for acute respiratory infections, PLoS One 7 (12) (2012) e51147.
[4] Y. Zhang, J. Zhang, H. Sheng, H. Li, R. Wang, Acute phase reactant serum amyloid A in inflammation and other diseases, Adv. Clin. Chem. 90 (2019) 25–80.
[5] V. Prendki, A. Malezieux-Picard, L. Azurmendi, J.C. Sanchez, N. Vuilleumier, S. Carballo, X. Roux, J.L. Reny, D. Zekry, J. Stirnemann, et al., Accuracy of C-reactive protein, procalcitonin, serum amyloid A and neopterin for low-dose CT-scan confirmed pneumonia in elderly patients: a prospective cohort study, PLoS One 15 (9) (2020) e0239606.
[6] X. Jiao, T. Peng, Z. Liang, Y. Hu, B. Meng, Y. Zhao, J. Xie, X. Gong, Y. Jiang, X. Fang, et al., Lateral flow immunoassay based on time-resolved fluorescence microspheres for rapid and quantitative screening CA199 in human serum, Int. J. Mol. Sci. 23 (17) (2022).
[7] X. Jing, S. Hong, J. Zhang, X. Yang, X. Geng, Y. Ye, Z. Hu, A rapid and quantitative detection method for plasma soluble growth stimulating gene protein 2 based on time resolved fluorescence immunochromatography, Analytical methods : advancing methods and applications 14 (22) (2022) 2179–2187.
[8] B.J. Langford, M. So, S. Raybardhan, V. Leung, D. Westwood, D.R. MacFadden, J.R. Soucy, N. Daneman, Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis, Clin. Microbiol. Infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 26 (12) (2020) 1622–1629.
[9] H.M. Rowe, V.A. Meliopoulos, A. Iverson, P. Bomme, S. Schultz-Cherry, J.W. Rosch, Direct interactions with influenza promote bacterial adherence during respiratory infections, Nature microbiology 4 (8) (2019) 1328–1336.
[10] S. Zhu, C. Zeng, Y. Zou, Y. Hu, C. Tang, C. Liu, The clinical diagnostic values of SAA, PCT, CRP, and IL-6 in children with bacterial, viral, or Co-infections, Int. J. Gen. Med. 14 (2021) 7107–7113.
[11] L. Gao, X. Liu, D. Zhang, F. Xu, Q. Chen, Y. Hong, G. Feng, Q. Shi, B. Yang, L. Xu, Early diagnosis of bacterial infection in patients with septicopyemia by laboratory analysis of PCT, CRP and IL-6, Exp. Ther. Med. 13 (6) (2017) 3479–3483.
[12] Q. Do, T.M. Dao, T.N.T. Nguyen, Q.A. Tran, H.T. Nguyen, T.T. Ngo, Procalcitonin identifies bacterial coinfections in Vietnamese children with severe respiratory syncytial virus pneumonia, BioMed Res. Int. 2020 (2020) 7915158.

[13] L. Perez, Acute phase protein response to viral infection and vaccination, Arch. Biochem. Biophys. 671 (2019) 196–202.
[14] G. Bozlu, H. Tanriverdi, G. Aslan, N. Kuyucu, The value of acute phase reactants and LightCycler(R) SeptiFast test in the diagnosis of bacterial and viral infections in pediatric patients, Archivos argentinos de pediatria 116 (1) (2018) 35–41.
[15] M. Li, Y.J. Qin, X.L. Zhang, C.H. Zhang, R.J. Ci, W. Chen, D.Z. Hu, S.M. Dong, A biomarker panel of C-reactive protein, procalcitonin and serum amyloid A is a predictor of sepsis in severe trauma patients, Sci. Rep. 14 (1) (2024) 628.