Research Article

Evaluation of Proflo-U® Platform for Urine Albumin Measurement in Chronic Kidney Disease Diagnosis: A Comparative Study

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Article Info

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Keywords

Chronic kidney disease (CKD), Albuminuria, Point-of-care (PoC) solutions, Proflo-U® platform, Fluorescence-based measurement, Immunoturbidity, Diagnostic accuracy

Abstract

Background: Chronic kidney disease (CKD) presents a global health challenge, requiring efficient assessment tools for effective management. Albuminuria assessment serves as a crucial indicator of CKD diagnosis, stage-classification, and progression risk. However, for the large-scale screening, the current laboratory-based methods lack portability and entail delays. Point-of-care (PoC) solutions like dipsticks offer promise, but sensitivity limitations persist.

Objective: To address this gap, we evaluated Proflo-U®, a novel fluorescent-based urine albumin measurement technology with the potential for PoC deployment, with the immunoturbidity-based Beckman Coulter system.

Results: Our study, based on a blinded comparison of 255 patient samples, revealed a high correlation (R2>0.9) between Proflo-U® and Beckman Coulter based measurement. Proflo-U® has been able to demonstrate comparable diagnostic accuracy, with strong sensitivity and specificity across different urine albumin concentration categories. Statistical analyses supported its reliability, and Receiver Operating Characteristic (ROC) analysis highlighted its clinically acceptable diagnostic accuracy.

Conclusion: Our findings suggest that Proflo-U® holds potential for mass screening initiatives in resource-limited settings to enable early CKD detection and management.

Introduction

Chronic Kidney Disease (CKD) is rapidly emerging as a significant global public health concern, placing an escalating burden on healthcare services and infrastructure worldwide [1]. Recognized by the Kidney Disease Improving Global Outcome (KDIGO) initiative, CKD is characterized by persistent abnormalities in kidney structure or function, lasting for more than three months, with profound implications for overall health. Key indicators used for CKD assessment based on function, include albuminuria levels, reflecting kidney damage, and estimated glomerular filtration rate (eGFR), indicative of kidney function [2]. These metrics serve as cornerstones for risk stratification and tailored management strategies, facilitating optimal allocation of healthcare resources and expediting referrals for patients at elevated risk of CKD progression.

Remarkably, even in the early stages of CKD, when eGFR levels may remain within normal or partially elevated ranges, the presence of mildly elevated level of albumin in urine emerges as a significant prognostic marker, impacting both diabetic and non-diabetic patient populations [3]. Alongside the recommendations set forth by organizations such as KDIGO, The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI), American Diabetes Association, European Association for the Study of Diabetes, and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) advocate for routine albuminuria screening, particularly in individuals with diabetes mellitus [4–6][7]. Notably, among diabetic patients with nephropathy, albuminuria consistently emerges as a robust predictor of End-Stage Renal Disease (ESRD), underscoring its clinical significance [5].

Moreover, heightened surveillance through more frequent albuminuria screening is advised for patients at increased risk of kidney disease progression, such as those with hypertension or cardiovascular disease, as well as individuals exhibiting evidence of worsening kidney damage. The primary advantage offered by urine albumin estimation as diagnostic marker is its non-invasive nature of sample while eGFR estimation either with creatinine or cystatin C is a serum biomarker and hence associated with invasive blood drawing. However, CKD that is 'not' associated with nephron or tubular damage does not show urine albumin increase at the initial stage. Moreover, the eGFR creatinine marker vary across individual based on the race, ethnicity, and muscle mass. A new biomarker i.e. Cystatin C that is associated with renal functional status, also shows elevated levels in inflammatory states and thyroid dysfunction independent of kidney disease [8]. Albuminuria is categorized into A1, A2, and A3 based on the daily excretion of albumin in urine. A1, representing levels below 30mg/24 hrs, is considered within the normal to mildly increased range. A2, ranging from 30 to 300mg/24hrs, denotes a moderately increased level, while A3, exceeding 300mg/24hrs, signifies severe elevation [9]. Interestingly, urine albumin as a biomarker is associated with different kidney disease however, the timeline of albumin increase can classify condition. For example, in case of proximal tubular nephrotoxin or acute kidney injury (AKI), there is a rapid increase in urine albumin over a short period of time that might stabilize or recover upon management. While in case of CKD, the urine albumin concentration increases gradually over a longer course of time. The latest KDIGO guideline suggests if the urine albumin level has been persistently elevated (> 30 mg/g) for greater than 3 months should be diagnosed as CKD [10,11].

While laboratory-based techniques like immunoturbidimetry, nephelometry, Flow Injection Analysis (FIA), and Sequential Injection Analysis (SIA) offer highly accurate results, their implementation is restricted to centralized laboratory settings, leading to prolonged turnaround times for patient reports [12]. To address the need for timely and accessible diagnostics, recent advancements have introduced point-of-care solutions utilizing reader devices and dipstick technology. However, conventional dipsticks exhibit limitations in sensitivity compared to quantitative methods, compromising diagnostic accuracy, particularly in detecting lower levels of albuminuria. In one large study, a protein dipstick result of trace or higher was associated with ACR values ≥30 mg/g (≥3 mg/mmol) with a sensitivity of only 69.4% and 86.8% specificity [13]. Though, easy to use and PoC deployable however, desirable diagnostic process should have high specificity and sensitivity both at A2 and A3 range while having other features likes ease of use and affordability that favors PoC deployment. Such a system will enable mass screening for early diagnosis and monitoring at resource limited setup. The Proflo-U® albumin test is expensive than the multi-parameter semi-quantitative urine dipsticks as PoC solution. However, the later has the major disadvantage of being poor sensitivity at the lower range of albumin, i.e., below 300mg/L resulting in missing of early stages of CKD patients during mass screening. Further, the readout of the test are overlapping colour indicator, that are difficult to objective estimate using visual inspection, corresponding broad range of concentration instead of a quantitative value (that necessitates the use of a relatively expensive reader). Nonetheless, if we compare the costing with the quantitative albumin estimation PoC solutions like Siemens DCA microalbumin/creatinine test and Abbott Afinion ACR test, Proflo-U® test is marginally lesser in price and comparatively has broader range of detection. Proflo-U® analytical linear range is 20-1000 mg/L while the other products have 5-200 mg/L, which is a major advantage in case of nephrological conditions. In addition, the reader device is battery operated and easy to use ad IoT enabled that offers a large range of advantages in data storage, remote maintenance, and automated operational qualifications. The innovative fluorophore nanosensor based technology has advantage over immunoturbidity be being highly thermostability, which alleviates the major limitation of cold storage and cold chain logistics in mass screening at resource limited settings [14].

To bridge this diagnostic gap, we investigated the patented

Proflo-U® platform and compared with the laboratory based immunoturbidity method for the analytical performance. Our previous published study demonstrated that Proflo-U® offers comparable albuminuria estimation to established reference standards, such as the Beckman Coulter system and Biosense assay, with a high correlation coefficient ($R2 > 0.99$, $p > 0.05$). Nevertheless, our evaluation was constrained by the utilization of spiked samples containing recombinant Human Serum Albumin (r-HSA) [14]. To ascertain the true diagnostic utility of the Proflo-U® platform, we conducted further analysis using urine samples obtained from a cohort of 255 hospitalized patients, following approval from both the research council and ethical committee at AIIMS Bhubaneswar, India. Blinded testing was performed to validate its efficacy in real-world clinical settings.

Material and Methods

Study Design

Sample type

The sample type was a 24 hrs. urine sample provided to the AIIMS Bhubaneswar Biochemistry Department for urine albumin analysis from the admitted patients in the hospital.

Sample Size

An n=238 + 20 sample size has been calculated considering the prevalence of at least 50% of the sample will have diagnostically relevant level of albumin to determine the study method at 95% Confidence of Interval with 85% sensitivity and specificity and 90% precision as parameter for calculation.

Sample exclusion criteria

The exclusion criteria exercised for the urine samples to be tested were: 1. Urine samples with blood contamination, 2. Urine samples with dark amber color appearance and 3. Urine samples opaque and dense or preidentified UTI infection.

Study Period

The study period was between 23rd November 2021 to 8th March 2022. The samples have been run parallelly both in the Beckman Coulter as well as Proflo-U® platform and the data has been recorded from both the system along with the patient ID.

The study design has been reviewed and passed by the AIIMS Bhubaneswar Institutional Ethics Committee Ref No. T/IM-NF/Biochem/21/74. All studies involving human subjects have been conducted in compliance with the ethical principles for medical research involving human subjects, in accordance with the Declaration of Helsinki.

Sample analysis Method

The urine samples were coded with Hospital's Patient ID number created through the Laboratory Information Management System (LIMS). The sample freshly received by the Biochemistry department have been parallelly analyzed with Beckman Coulter Microalbumin reagent from Ireland, OSR6167 Lot no 2312 on Beckman Coulter AU5800 fully automated chemistry analyzer, S/N 2013081121, by immunoturbidity inhibition assay, according to manufacturer instruction and Proflo-U® cartridge on Proflo-U® platform according to manufacturer instruction [14]. The test has been conducted at NABL accredited AIIMS Bhubaneswar Biochemistry Laboratory. The albumin concentration obtained for each sample were noted with the patient ID both from Beckman Coulter and Proflo-U®.

Data analysis

The data has been statistically analyzed for method correlation with R language using shiny [15]

web application framework for the Passing Bablock regression and Bland Altman (BA) plot. The Receiver Operating characteristic (ROC) in R studio package [16].

Results and Discussion

The sample size for the study was determined according to the guidelines for Sample Size Estimation for Diagnostic Accuracy Studies, where a new diagnostic test is compared with the reference standard in a cohort provided the true disease status and prevalence are known [17]. With a fixed type I error of 0.05, a marginal error of up to 10%, and a confidence interval of 95%, the prevalence of CKD was estimated at approximately 12% (the mean reported prevalence of CKD in India ranging from 4% to 20%) [18]. Targeting a sensitivity and specificity of at least 92%, a minimum sample size of 236 was calculated [19, 20]. Permission for a sample size of 238 + 20 was obtained from the Institutional Ethics Committee. A similar sample size was utilized for the analysis of the HemoCue point-of-care system, with n=259 [21] and n=108 urinary samples were analyzed for comparison of 5 immuno-turbidimetric methods for urine albumin quantification [22].

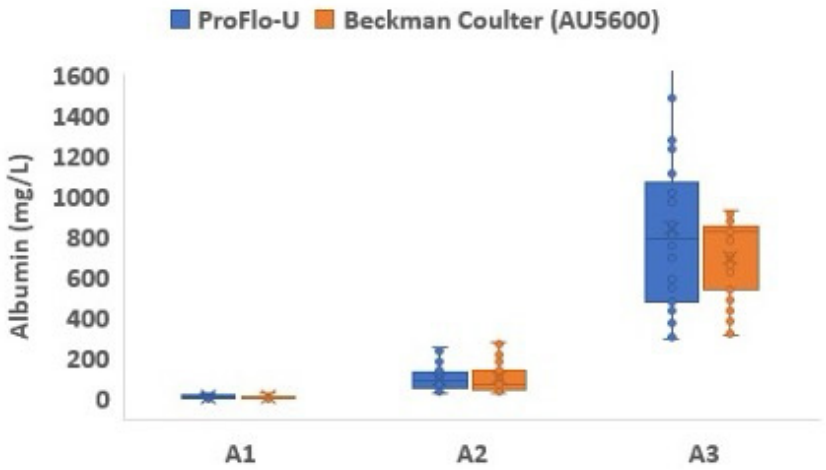
A total of 258 urine samples received at the AIIMS Bhubaneswar Biochemistry Department for urine microalbumin analysis were used for the study. Three samples lacked patient IDs and were therefore excluded, leaving n=255 urine samples for the analysis. No samples were lost, as testing was conducted promptly upon receipt by the Biochemistry Department. Results for urine albumin concentration in mg/L were tabulated (Supplementary Table 1).

The distribution of the samples between normal and elevated were almost equally represented, as 138 samples have shown below 30mg/L and 117 samples above 30mg/L concentration for the urine albumin by the Beckman Coulter System. Though, the immunoturbidity method Beckman Coulter System is not a gold standard in true sense but can be regarded as the best test under "reasonable conditions" and hence been considered as the reference method.

The urine samples have been further divided into three categories normal (A1) <30mg/L, moderately high (A2) >30mg/L but <300mg/L and severely high (A3) > 300mg/L (We have used annotation A1, A2 and A3 that generally been used for urine albumin creatinine ratio, but in this case with reference to 24 hrs

urine albumin) both for the test method Proflo-U® platform and the reference method Beckman Coulter System. The distribution of the tested samples has been represented in the Box-Whisker plot (Figure 1). In the A1 category the reference method had determined 138 samples while 132 samples by the test method, suggesting 5 samples have been wrongly categorized. In the A2 category 77 samples have been identified by the reference method while the test method had shown 84, corresponding to a difference of 6. In the category severely high category reference method has identified 41 samples while the test method could pick 39 samples indicating a non-agreement of 2.

Figure 1: Box-Whisker Plot of the urine albumin measured samples within the A1, A2 and A3 categories by Proflo-U® and Beckman Coulter.



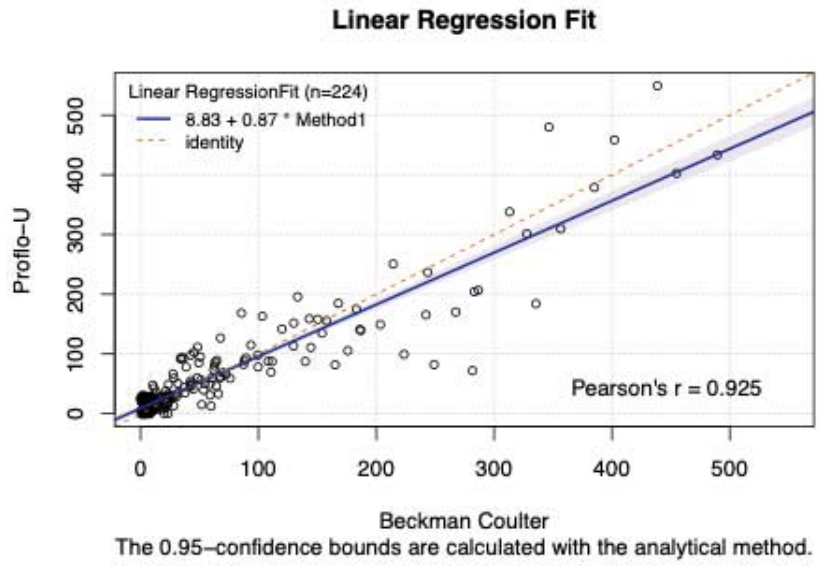
The sensitivity, specificity, positive prediction value (PPV) and negative prediction value (NPV) were calculated for each category keeping in each case the total sample size 255 (Table 1). The sensitivity with which Proflo-U® platform was able to detect the urine sample in the A1, A2 and A3 category with respect to the reference method were 94.2%, 97.37% and 95.12%, respectively. The obtained specificity with Proflo-U® platform for A1 =98.29%, A2 =94.41% and A3 =100%. In the referenced literature, the PoC urine albumin diagnostic methods compared with the laboratory based immune-nephelometry has reported comparable degree of sensitivity of 83.8% in semi-quantitative antibody-based urine albumin detection while 79.6% for the quantitative method and specificity were 93.8 and 97.1, respectively[23]. In different PoC methods for Albumin estimation the reported range for sensitivity was 86-98% and specificity were 61-94% [24]. The PPV obtained for the Proflo-U® platform for A2 was lowest with 90.5% while highest for the A3 category with 100%, similarly, the lowest obtained NPV was for the A1 category with 93.1% and highest in A3 with 99.1%. The literature reported PoC diagnostic tests has shown PPV, 95.6% for quantitative and 88.6% for the semi-quantitative method, while NPV were 85.8% for quantitative and 91% for semi-quantitative method.

Table 1: Presenting the distribution of sample based on urine albumin content categorized as A1 (<30mg/L), A2 (30-300mg/L) and A3 (>300mg/L) with Beckman Coulter and Proflo-U® method. The calculated sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) in percentage for the Proflo-U® with Beckman Coulter estimation as the reference method has been tabulated.

		Beckman Coulter			
		A1 (<30mg/L)	**A2 (30-300mg/L)**	**A3 (>300mg/L)**	**Total**
Proflo-U	**A1 (<30mg/L)**	130	2	0	132
	A2 (30-300mg/L)	8	74	2	84
	A3 (>300mg/L)	0	0	39	39
	Total	138	76	41	255
1	**Sensitivity%**	94.2	97.37	95.12	
2	**Specificity%**	98.29	94.41	100	
3	**PPV%**	98.5	90.5	100	
4	**NPV%**	93.5	98.8	99.1	

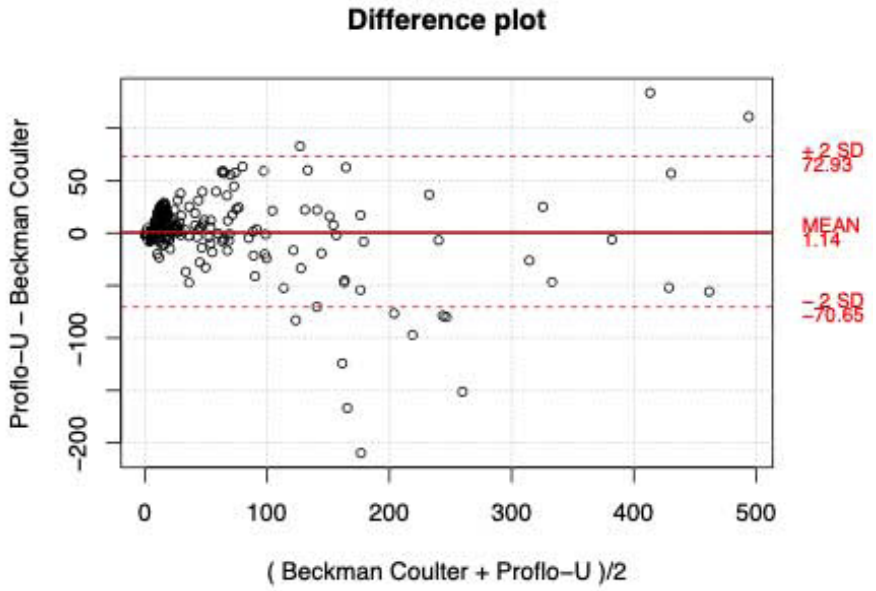
Considering the quantitative nature of both the test and reference measurement technologies, we evaluated agreement of analytical methods and possible systematic bias between them with Passing Bablok regression. Results are presented with scatter diagram and regression line where the sample size considered n=224 (samples considered with urine albumin content less than 500 mg/L, considering the reference method highest claimed analytical range 5-300 mg/L)[25] Figure 2 (The analysis for the complete cohort pool with sample size n=255 has been provided in the Supplementary Figure 1). The Pearson coefficient in both the cases are >0.9 (r=0.916 for n=255 and r=0.925 for n=224) indicating very strong relationship between the data obtained from test and reference methods.

Figure 2: The Passing Bablok Regression fit has been presented for the all the n =224 samples for Proflo-U® and Beckman Coulter.



The data next analyzed with the Bland Altaman plot for sample size n=255 (Supplementary Figure 2) and sample size n=224 Figure 3. The mean offset for n=224 data points was +1.14 for Proflo-U® method over Beckman Coulter where the 95% confidence Interval the Lower bound was -70.65 and upper bound is +72.93. If we consider all the data points (n=255), the data points at a range 600 above show high degree of disagreement as the range is much beyond the analytical range of the reference method and as claimed by the manufacturer might show 'Prozone or hook effect' at albumin concentration >600mg/L (Supplementary Figure 2).

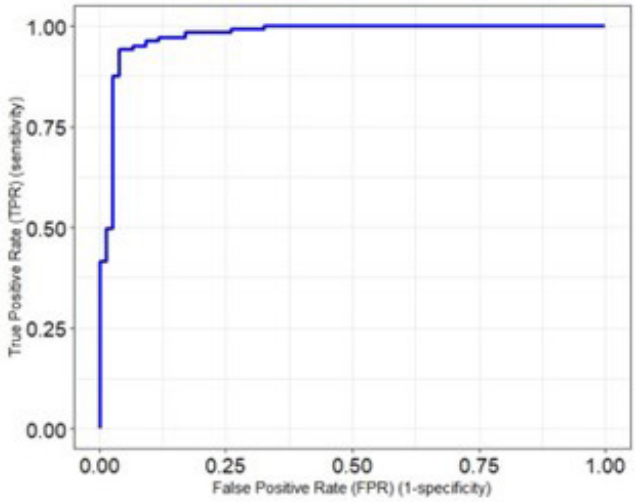
Figure 3: Bland-Altaman plot for method correlation where Proflo-U® serves as test method and Beckman Coulter as the reference method for sample size n =224.



To determine the diagnostic accuracy of the Proflo-U® we further analyzed the Receiver Operating characteristic (ROC) in two sets, where the set 1 for A1 and A2 category (Figure 4 A) and set 2 for A2 and A3 category (Figure 4 C). The samples were categorized based on the values obtained with the reference method Beckman Coulter as A1, A2 and A3. The data obtained by the Proflo-U® platform for the sample categorized as A1 was considered as normal and A2 as diseased for set 1. In set 1 there were total sample size was n=222 for which the ROC was analyzed. The Area Under Curve (AUC) was 0.977 with a cutoff at 30.6mg/L, where the specificity obtained 96%, sensitivity 94%, PPV= 0.977 and NPV= 0.90 Figure 4A. The response under different cut off values has been presented in Figure 4B. In set 2 the data obtained by the Proflo-U® platform for the sample categorized as A2 was considered as normal and A3 as diseased, where the sample size n=125 for which the ROC was analyzed. The Area Under Curve (AUC) was 0.998 with a cutoff at 253mg/L, where the specificity obtained 97.5%, sensitivity 100%, PPV= 0.987 and NPV= 1.00 Figure 4C. The response under different cut off values has been presented in Figure 4D.

Figure 4: The Receiver Operating Characteristic (ROC) curve was generated to assess the diagnostic accuracy. (A) Patient urine samples measured by the Proflo-U® platform for the prediction of A2 or urine albumin concentration range 30-300mg/L and A1 or urine albumin concentration range <30mg/L, the classification is based on the measured value obtained with the reference method Beckman Coulter. (B) Sensitivity, specificity, Positive Predictive Value and Negative Predictive Value at different cutoff for the Response Operating Curve for the data set corresponding to A1 and A2 categories. (C) Patient urine samples measured by the Proflo-U® platform for the prediction of A3 or urine albumin concentration range >300mg/L and A2 or urine albumin concentration range 30-300mg/L, the classification is based on the measured value obtained with the reference method Beckman Coulter. (D) Sensitivity, specificity, Positive Predictive Value and Negative Predictive Value at different cutoff for the Response Operating Curve for the data set corresponding to A2 and A3 categories.

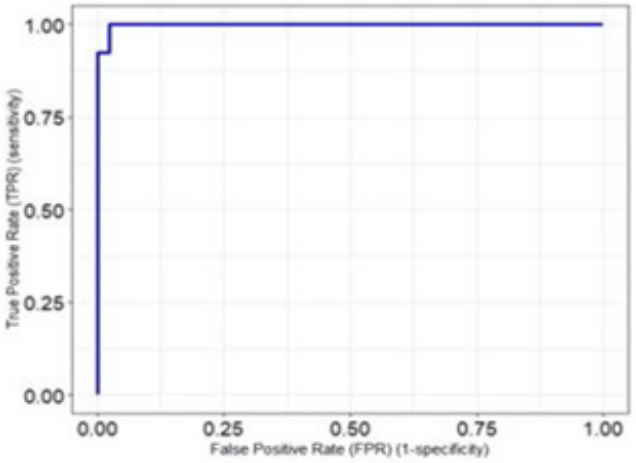
(A)



(B)

Cut Off	Sensitivity	Specificity	PPV	NPV
67.72	1.00	0.68	0.85	1.00
59.45	0.99	0.74	0.87	0.98
48.89	0.99	0.83	0.91	0.97
43.69	0.97	0.88	0.94	0.94
38.69	0.96	0.91	0.95	0.93
33.84	0.95	0.94	0.96	0.91
30.63	0.94	0.96	0.98	0.90
28.42	0.88	0.97	0.98	0.82
15.04	0.50	0.99	0.99	0.52
12.12	0.42	1.00	1.00	0.49

(C)



(D)

Cut Off	Sensitivity	Specificity	PPV	NPV
253.35	1	0.97	0.99	1
179.47	0.92	1	1	0.87

Urine albumin is an important measurement procedure used for diagnosis, risk classification, and management of CKD. The increasing prevalence of CKD can be controlled only through early diagnosis. Population level mass screening at point of care can be a major driver for this initiative. In the previous publication, Proflo-U® platform has been found suitable for the PoC deployment. This study evaluated the performance of the novel fluorescence-based point-of-care system Proflo-U® with the reference method laboratory based immunoturbidity Beckman Coulter using patient urine sample as test specimen. In the sample size 255, it has been found that the Proflo-U® platform has high correlation with the reference method and diagnostic accuracy. Suggesting, the Proflo-U® platform has the potential for application as the diagnostic method for the urine albumin measurement.

Conclusion

The evaluation aimed to assess the Proflo-U® platform's performance in urine albumin measurement for CKD diagnosis. Utilizing patient urine samples, the Proflo-U® platform demonstrated comparable accuracy to the reference method, Beckman Coulter System, with high correlation coefficients. Despite initial limitations with synthetic samples, validation using real patient samples confirmed its efficacy in clinical settings. Sensitivity and specificity analyses showed strong performance of the Proflo-U® platform across different

albuminuria categories, aligning well with existing literature. Statistical analyses further supported its reliability, with strong agreement between methods. Receiver Operating Characteristic (ROC) analysis highlighted the Proflo-U® platform's high diagnostic accuracy, indicating its potential for early CKD detection and management, particularly in resource-limited settings. Further validation studies are recommended to ensure widespread adoption of this innovative point-of-care solution.

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Contributors

MHS has conducted the Proflo-U® platform and Beckman Coulter based experiments and collected the data. SM conducted all the Biosystem based experiments and collected the data. DB has designed the study and analyzed the data. MHS, SM and DB has prepared and reviewed the manuscript. DB was responsible for overall supervision of the project and review of the final paper.

Supplementary Table 1: Cohort sample n=255 with Patient ID and measured values from Proflo-U® platform (PFL) and Beckman Coulter system (BC).

S.No.	Patient ID	PFL (in mg/L)	BC (in mg/L)
1	11230570	1637.3	854.86
2	11230780	8.08	11.6
3	11230947	0	4.14
4	11230860	0	7.87
5	11240718	1017.2	853.42
6	11240458	28.02	24.45
7	11240695	974.27	837.57
8	11240666	99.37	223.57
9	11240691	7.23	4.62
10	11250639	13.08	28.14
11	11250526	149.15	203.39
12	11250761	0	7.52
13	11250387	15.07	51.97
14	11250648	0	20.18
15	11250342	820.8	720.74
16	11250535	87.39	111.55
17	11250414	1726.07	843
18	11250653	80.26	62.86
19	11250477	0	3.72
20	11250840	301.33	327.63
21	11250834	98.23	99.6
22	11260277	56.44	51.02
23	11260339	16.64	23.35
24	11260168	34.63	37.66
25	11260331	206.63	286.68
26	11260801	71.98	281.68
27	11260584	12.51	59.85
28	11260456	10.51	21.64
29	11260547	0	23.35
30	11260560	0	6.45
31	11300180	27.14	4.2

32	11300318	27.71	5.67
33	11300196	378.87	385.069
34	11300205	433.64	489.53
35	11300188	93.18	36.24
36	11300612	157.93	150.38
37	11300585	184.89	167.82
38	11300478	1483.83	876.22
39	11300431	195.73	133.21
40	11300420	78.06	38.58
41	11300435	40.98	44.75
42	11300462	309.69	356.51
43	11300580	28.89	15.76
44	11300532	9.6	10.75
45	11300537	47.54	42.91
46	12010251	26.57	26.05
47	12010240	3.72	8.82
48	12010193	338.08	313.13
49	12010296	25.43	4.44
50	12010196	89.18	87.94
51	12010244	26.43	20.38
52	12010140	82.62	87.47
53	12010159	48.96	58.73
54	12010173	16.44	15.1
55	12010606	1111.85	874.4
56	12010237	595.52	541.19
57	12010422	14.59	6.9
58	12010574	29.28	24.33
59	12010513	21.72	7.63
60	12010569	60.09	48
61	12010681	29.8	22.58
62	12010568	87.76	108.14
63	12020381	1.18	4.2
64	12020642	139.39	186.93
65	12020344	5.75	7.55
66	12020463	19.2	16.8
67	12020353	26.43	8
68	12020555	91.89	33.82
69	12020417	3.07	4.6
70	12020338	1761.82	860.03
71	12020368	54.81	42.48
72	12020232	0.75	3.51
73	12020636	134.68	154.05
74	12020484	45.4	42.34
75	12020145	549.31	438.54
76	12020138	12.73	8.38
77	12030254	787.36	842.59

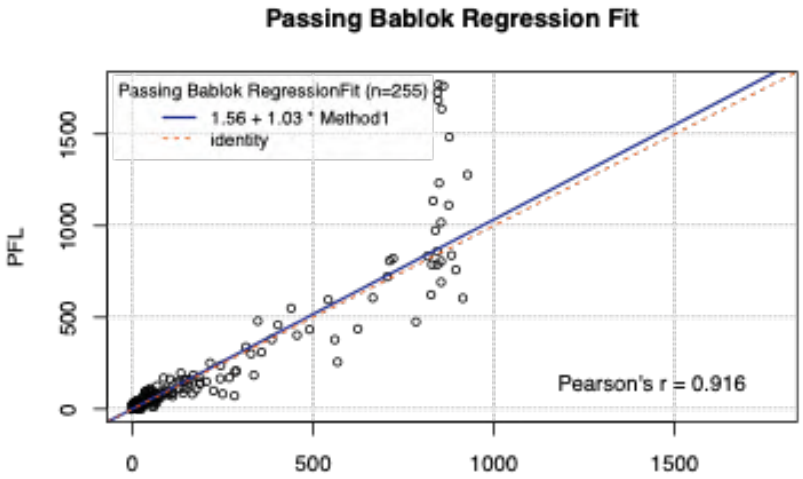
78	12030261	17.25	12.79
79	12030214	50.39	54.53
80	12030478	0	4.54
81	12030444	250.79	214.3
82	12030288	9.03	5.29
83	12030612	1.61	5.83
84	12030364	13.73	6.15
85	12030248	7.88	8.06
86	12030270	436.78	623.05
87	12030295	1135.53	831.37
88	12030288	1685.08	845.14
89	12030456	141.96	119.94
90	12030299	25.71	21.49
91	12030630	61.94	67.73
92	12030240	7.79	12
93	12030284	458.74	402.08
94	12080122	721.18	704.55
95	12080235	10.45	6.01
96	12080185	0	7.1
97	12080192	168.34	85.58
98	12080210	3.58	4.83
99	12080401	15.87	4.61
100	12080199	28.71	6
101	12080358	1768.95	846.11
102	12100550	7.88	13.64
103	12100548	10.02	6.68
104	12100429	27.57	9.41
105	12100559	89.04	64.71
106	12100445	479.99	346.42
107	12100493	44.68	37.37
108	12100619	158.93	143.07
109	12100568	5.57	7.24
110	12100593	26.57	10.56
111	12100526	758.98	894.36
112	12100636	1277.73	926.69
113	12100405	15.02	20.07
114	12140249	170.34	267.47
115	12140169	33.13	66.01
116	12140315	15.27	19.56
117	12140299	21.58	0.99
118	12140275	46.11	64.38
119	12140232	0	1.94
120	12140173	606.22	664.62
121	12140290	87.47	139.76
122	12140128	4.32	2.67
123	12140317	47.96	10.34

124	12140490	165.49	242.19
125	12140373	42.69	11.38
126	12140238	163.21	103.32
127	12140336	15.73	7.54
128	12140516	18.44	4.84
129	12140408	29.14	1.55
130	12140433	622.91	825.79
131	12140334	25.43	23.56
132	12140428	78.2	99.72
133	12140441	0	2.85
134	12150324	140.82	185.96
135	12150421	111.58	48.4
136	12150451	0	4.42
137	12150519	0	3.93
138	12150570	0	1.15
139	12150347	28.57	2.1
140	12150302	113.29	129.81
141	12150192	174.76	183.1
142	12150186	204.29	283.16
143	12150164	0	0.72
144	12150168	16.01	19.91
145	12150216	27.43	10.14
146	12150479	19.87	0.68
147	12150238	26.14	2.47
148	12150216	24.14	10.14
149	12150633	25.86	1.07
150	12150219	20.29	1.27
151	12160439	4.6	0.01
152	12160437	839	882.43
153	12160411	0.61	0.54
154	12160455	1232.66	848.04
155	12160521	25.29	12.81
156	12160388	13.73	3.05
157	12160544	93.04	89.43
158	12160480	0	1.71
159	12160362	20.29	12.5
160	12160212	23.72	16.27
161	12160298	236.81	243.69
162	12160366	27.71	7.04
163	12160346	378.01	559.48
164	12160161	69.5	110.7
165	12160261	804.91	853.61
166	12160181	50.53	31.6
167	12160216	14.87	3.28
168	12170192	59.09	75.96
169	12170108	0	2.24

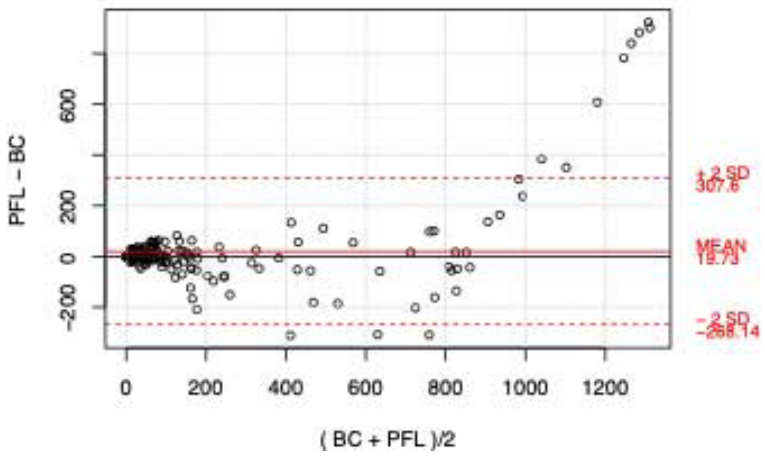
170	12170154	0	3.83
171	12170238	0.9	0.91
172	12170220	16.44	9.23
173	12170333	51.24	43.18
174	12170183	13.59	2.49
175	12170322	4	6.64
176	12170236	155.65	157.73
177	12170506	30.04	28.43
178	12170456	22.86	7.46
179	12170556	17.87	3.17
180	12170492	85.05	49.39
181	12170475	691.66	853.59
182	12170571	28.41	21.96
183	12170542	475.86	784.08
184	12170382	26.43	15.42
185	3030584	114.86	93.61
186	3030316	7.03	5.71
187	3030378	10.02	5.22
188	3030457	37.98	21.5
189	3030304	17.58	23.07
190	3030588	10.02	10.3
191	3040424	11.74	8.18
192	3040275	95.03	50.6
193	3040179	7.8	16.23
194	3040689	604.37	913.78
195	3040137	0	2.05
196	3040523	4.18	3.38
197	3040662	14.87	12.24
198	3040187	59.37	28.29
199	3040296	126.7	67.79
200	3040405	20.01	2.57
201	3040453	24.57	0.52
202	3050287	402.69	454.77
203	3050302	0	0.79
204	3050401	18.15	6.33
205	3050177	30.42	1.41
206	3050146	26.43	0.13
207	3050281	255.92	567.08
208	3050153	24.14	0.03
209	3050238	82.2	249.05
210	3050200	17.32	19.37
211	3050165	15.41	11.83
212	3070650	9.17	10.15
213	3070567	13.16	6.44
214	3070278	39.41	53.53
215	3070438	68.65	69.69

216	3070566	0	4.31
217	3070573	0	4.74
218	3070655	102.73	45.23
219	3070824	81.91	165.06
220	3070455	65.22	72.49
221	3070736	30.85	58.93
222	3070333	184.18	335.44
223	3070257	23	7.08
224	3070494	28.42	30.34
225	3070571	808.61	710.95
226	3070352	48.82	23.67
227	3070392	6.03	8.92
228	3070217	66.79	27.48
229	3070286	23	3.11
230	3070532	29.85	3.48
231	3080698	833.43	816.37
232	3080738	110.86	144.5
233	3080589	24.57	3.54
234	3080390	73.78	62.03
235	3080284	97.88	42.55
236	3080533	35.27	13.2
237	3080443	23.15	3.9
238	3080578	93.46	34.38
239	3080722	20.58	20.01
240	3080509	86.05	63.28
241	3080669	34.27	31.46
242	3080665	105.44	175.89
243	3080700	0	4.19
244	3080537	2.18	8.93
245	3080056	8.3	19.9
246	3080552	787.79	828.26
247	3080610	151.8	129.97
248	3080558	59.52	67.36
249	3080529	14.3	3.37
250	3080559	859.68	843.1
251	3080177	0	2.69
252	3080426	24.57	9.18
253	3080404	59.8	60.44
254	3080408	17.58	11.62
255	3080278	33.42	23.46

Supplementary Figure 1: The Passing Bablok Regression fit has been presented for the all the 255 samples for Proflo-U® and Beckman Coulter.



Supplementary Figure 2: The Bland-Altaman plot has been presented for the all the 255 samples for Proflo-U® and Beckman Coulter.



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