YENEPOYA

(DEEMED TO BE UNIVERSITY)
Recognized under Sec 3(A) of the UGC Act 1956
Accredited by NAAC with 'A' Grade

Details of the Collaborative Activity

2019-2021

Name of the Collaborating Institute: Prantae Solutions Pvt. Ltd., Bhubaneshwar

Name of the Collaborating Department: Yenepoya Medical College Hospital

Activities:

Clinical Trail Project:

A clinical agreement was signed between the institutes Prantae Solutions Pvt. Ltd., Bhubaneshwar and Yenepoya Medical College Hospital on 21st November 2019.

As a part of the study, YIT provided microalbumin testing services to Dr. Raghavendra Rao, YMC for the Project titled "Evaluation of a fluorescence-based urine Albumin analysis and comparison with the gold standard with human urine sample"

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Annexure I

Clinical Investigation Plan

Title of the Clinical Investigation

Evaluation of a fluorescence based urine albumin analysis (CDSCO Test License: **MFG/TL/IVD/2019/000098**) and comparison with the gold standard (currently practiced method in the Yenepoya pathological lab) with human urine sample.

Clinical Investigation Number

PS/YU/MA_CT001

Version/Date

Version 1.0
Date: 01/12/2019

Sponsor

Prantae Solutions Private Limited (OPC)
Odisha, India.

Principle Investigator, coordinating Investigator and Investigation site

PI:	Dr. Raghavendra U
Co-PI:	Dr. M.H. Sherif
	Dr. Rekha P.D.
Investigation Site:	Central Laboratory, Yenepoya Medical Hospital, Deralakatte, Mangalore – 575018.

Introduction

Urine albumin content is one of the well-established non-invasive biomarkers for various clinical conditions. Increasing evidence towards the chronic kidney disease (CKD) and, in particular, the cardiovascular risks that CKD imposes, more sensitive detection of albumin in urine are required[1]. The most common method of urine albumin measurement is (94%) immunoassay-based of which mostly (85%) immuno-turbidimetric[2]. However, it poses certain limitation like, high cost, storage condition and sensitive only to immunologically active form of albumin. Albumin in the urine is exposed to a wider range of pH and ionic strength than found in plasma; other potentially modifying factors include the presence of high concentrations of urea,

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glucose and ascorbate, and cleavage by peptidases[3]. Thus, there may chances of under-representation of the urine albumin[4] and hence in the diagnosis. Thus, it is vital to research and experiment new methods to exploit the possibilities to overcome such bottlenecks that exist in the presently practiced methods. We propose an innovative patented technology based on fluorescent dye to quantify urine albumin from a range covering micro-albumuniuria to proteinuria.

Objective of the study

Objective 1: To compare between a novel urine protein analysis kit (under CDSCO Test License: **MFG/TL/IVD/2019/000098**) and gold standard (immuno-turbidometric method) for urine micro-albumin quantification with urine sample under clinical setting.

Objective 2: To analyze the data obtained from the two methods of measurements to determine the sensitivity, specificity, LOD and correlation coefficient and comparative analysis with the gold standard (immuno-turbidometric method).

Need for the study

The present immunological methods have certain drawbacks beside the cost and storage conditions that might impact the diagnosis of the disorder. An alternative to immunological method that not only reduce the cost of test and need for special storage condition but also able to detect total albumin content of the urine not just limited to the immune-reactive species of albumin is developed. Therefore, upon extensive screening, a newer fluorochrome has been identified with high specificity towards the albumin at the same time non-responsive to the urine microbial load, pH and other metabolites. This has been transformed into a cartridge for simple usage and analysis.

Research Question

The question to be addressed through this research are

1) Does the novel urine analysis kit is capable of estimating the amount of albumin in urine?
2) What is the level of accuracy of estimation of albumin in urine with novel urine analysis kit in comparison to the gold standard (immuno-turbidometric method)

Justification for the study

Kidney disorder is one of the major global healthcare burdens, where the prevalence rate is 10% and still growing. It has been noted that the kidney-disorder most often progress silently without any associated clinical symptom manifestation. As a consequence in majority of the cases it progresses undiagnosed till it reaches the terminal or irrecoverable stage.

Urine micro-albumin has been one of the well-established biomarkers for early identification of kidney damage. It is one of the routinely practiced methods under the

clinical settings. Presently, the microalbumin tests are primarily immunological method based either reporting as chromogenic color reaction as in Micral test or turbidimetric immunoassay.

We have developed a novel method with granted patent for urine albumin detection that is non-immunological method. This cost effective and simple method under laboratory condition is highly correlating with the gold standard like turbidimetric immunoassay. However, we understand that the method cannot be considered of any clinical relevance unless tested with real biological samples and made a head on comparison with the gold standard. Thus, a study will be conducted with patient/volunteer urine sample to do comparative analysis for the performance of the method for the purpose of urine micro-albumin analysis.

Study Design and Protocols

Study Duration
2-6 months

Study sample size
262 2* = 524 samples *In duplicates

Study Area
Yenepoya Medical College, Mangalore.

Study Sample
Urine (middle stream of the random urine)

Enrolment Procedure
1. Brief introduction of the study,
2. Matching of inclusion criteria
3. Informed consent form for participation in the study.

Inclusion Criteria
- Healthy Individuals with no previously known renal disorder history.
- Individuals within the age group of 18-45 years.

Exclusion Criteria
- Individual with clinically established renal disorder and /or
- Individual with suspected case of UTI and/or
- Individual who are pregnant

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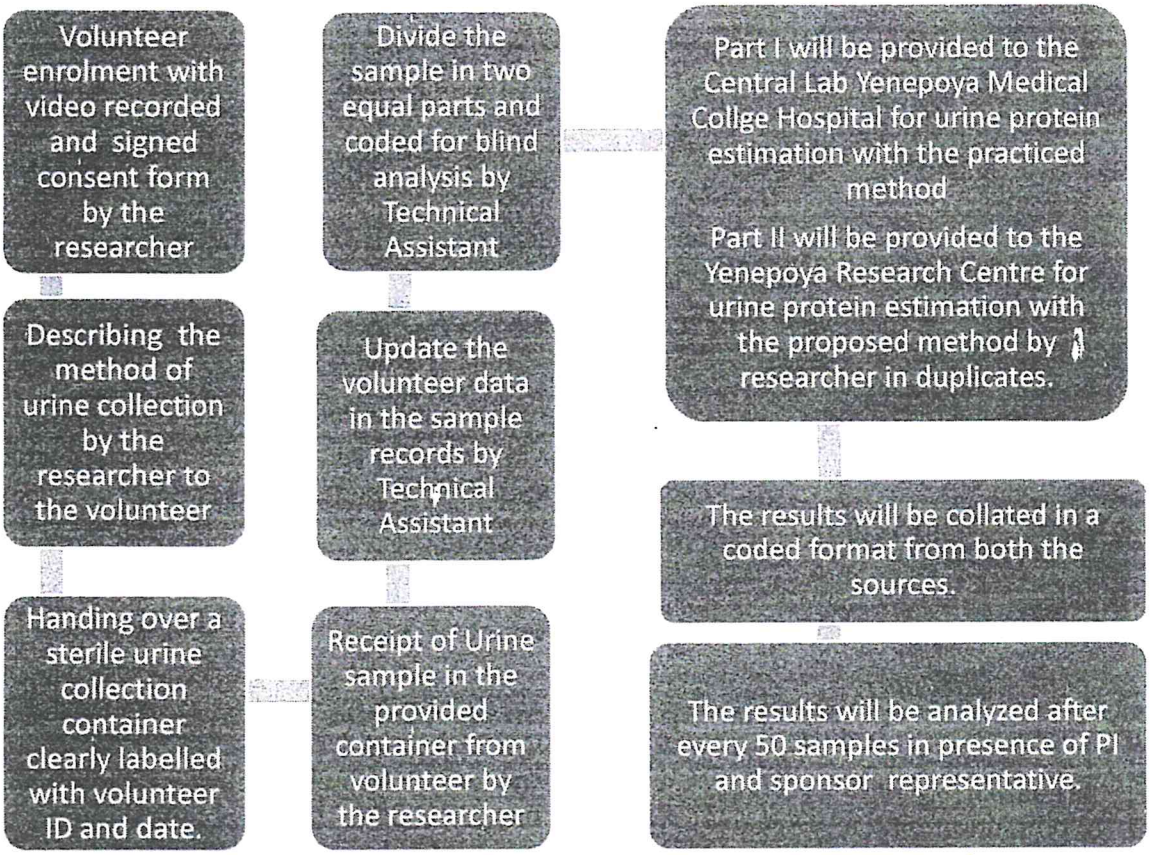
Flow chart to depict study design



Working protocols for sample analysis

Protocol for urine sample analysis using the cartridge (CDSCO Test License: MFG/TL/IVD/2019/000098)

1. Take out fresh cartridge from the sealed package [a].
2. Place the cartridge over a horizontal platform with its flat bottom
3. Remove the cap and add 1ml urine from the urine sample container from the mouth of the cartridge
4. Let it stand undisturbed for 40 seconds [b].
5. Put back the cap and shake it by gentle taping with finger on the walls (4-5 times).

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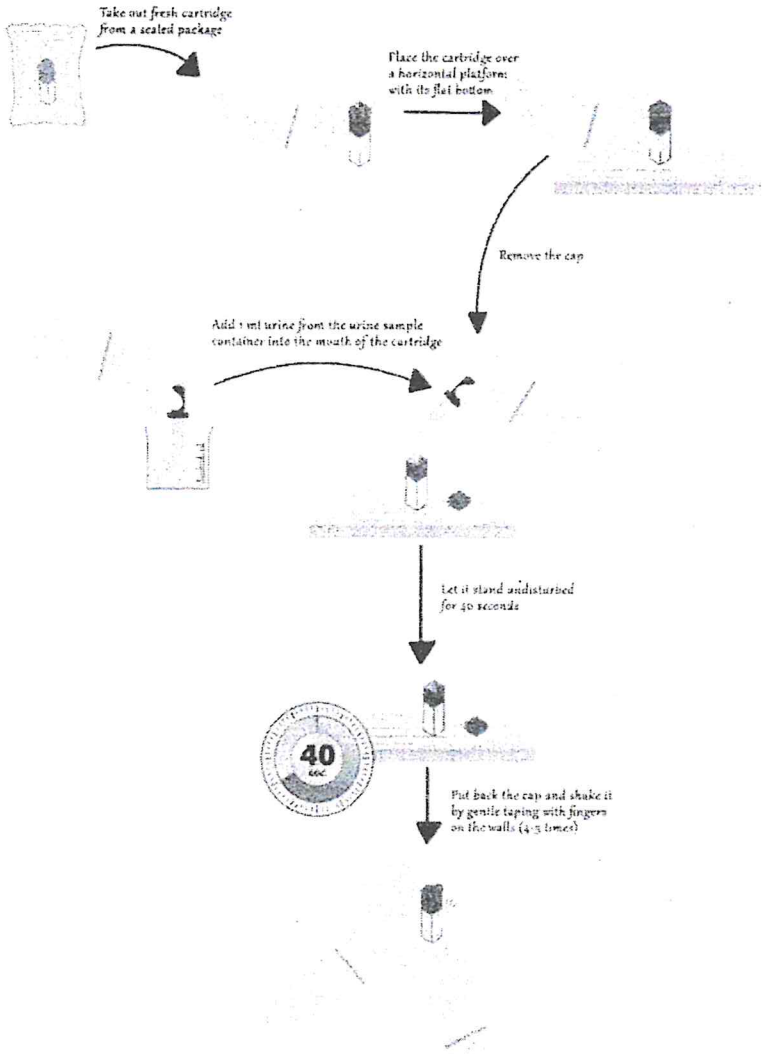
6. Take the reading in the Fluorescence spectrophotometer (PUDR2#0010.01) using the provided software (PUS2#0010.03).



Protocol for operation of Fluorescence spectrophotometer (PUDR2#0010.01) and use of the provided software (PUS2#0010.03).

1. Power on the Fluorescence spectrophotometer (PUDR2#0010.01) [c, d].
2. Open the software (PUS2#0010.03) and select for albumin measurement from the dashboard from the program [e].
3. Place the cartridge in the sample holder in the Fluorescence spectrophotometer.
4. Press the capture button on the dashboard.
5. Save the result in the folder with proper ID.

Notes

a: Ensure the package is properly sealed and not damaged and cartridge is in proper form. Note down the UID of the cartridge for records.
b. The time is required for filtration and should be checked by observing the amount of urine collected at the transparent bottom part of the cartridge.
c: The wire connection should be made proper and power should be fed from the appropriate power points
d: Fluorescence spectrophotometer should be powered on at least 2 minutes prior to operation in order to ensure proper stabilization of the laser.
e: Software should be properly opened and proper program selection should be made.

Data management

1. All the volunteer consent should be video recorded and stored.
2. All the volunteer consent forms should be properly filled, signed and stored.
3. All the collected volunteer information form details and sample ID should be stored in the prescribed format.
4. All sample results should be properly recorded with proper ID both in hardcopy (In the provided record notebook) and softcopy format.
5. All results should be presented with the proper ID after every 50 samples to the PI and representatives of sponsors for the analysis.
6. All Video recorded consents, consent forms and sample results should be handed over with proper ID both in hardcopy (In the provided record notebook) and softcopy format to the sponsor at the end of the project.
7. All test cartridges received from the sponsor should be indexed with their UIN.
8. All the packaged test cartridges received from the sponsor should be recorded for the quality audits

Clinical data collection

Not required for the proposed study.

Materials and equipment from sponsor

1. Disposable sterile urine collection containers volume 30 ml.
2. Disposable sterile cartridge for urine albumin quantification, manufactured under the CDSCO Test License: **MFG/TL/IVD/2019/000098**
3. Pipette P1000 Manual with an adjustable volume capacity of 100-1000 microliters.
4. Fluorescence spectrophotometer with customized software calibrated to estimate urine albumin content. (Name of the equipment: PUDR2#0010.01 Name of the software: PUS2#0010.03)

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Annexure II

Payment Schedule

The Institution has agreed to provide the services outlined in the table below to the Sponsor as per the Clinical Trial Agreement (CTA) and the charges are outlined accordingly.

Sl. No	Description	Total Cost
1	Test for micro albumin - Sample Handling Charges (524 samples @ Rs. 50)	26,200
2	Investigators fees	40,000
3	Site Coordinator fees	8,000
4	Contingency	2,000
Total		**76,200**

Any other services provided by either the Institution or its affiliated organisations including Yenepoya Foundation for Technology Incubation ("Incubator") will be costed extra and a consolidated invoice will be raised by the Incubator which is payable as per the terms and conditions outlined in the respective invoice.

The sponsor agrees to pay 60 % of the total costs before the initiation of the study and the rest 40 % is payable at the time of completion of the study.

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