# PREGNANT WOMEN WITH HYPERTENSION AND SELF-TESTING FOR PROTEINURIA: A CROSS-SECTIONAL STUDY

**Nirupama Palakodeti[1*] and Gopinath TV[2]**
**[1]Associate Professor, Department of Obstetrics &Gynecology, Sri Lakshmi Narayana Institute of Medical Sciences, Pondicherry – 605502**
**[2]Associate Professor, Department of Respiratory Medicine, Sri Lakshmi Narayana Institute of Medical Sciences, Pondicherry – 605502**

***Corresponding Author**
**Dr.Nirupama Palakodeti,**
**Associate Professor,**
**Department of Obstetrics &Gynecology,**
**Sri Lakshmi Narayana Institute of Medical Sciences,**
**Osudu, Agaram Village,**
**Pondicherry - 605502**

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**Abstract**

Test your own proteinuria during pregnancy in order to determine if your results are accurate. 172 pregnant women participated in the study. The spot protein-creatinine ratio (PCR) was estimated in the laboratory for pregnant women who self-tested in-clinic using visually readable dipsticks. The second index test included the use of an automated colorimeter as well as the testing by antenatal healthcare professionals. As a comparison to the primary reference test (PCR), sensitivities, specificities, negative predictive values and positive predictive values of self-testing, healthcare professionals, and colorimetric tests were calculated. In total, 167/172 (97%) of the samples had sufficient data for analysis. Based on a comparison between self-testing and PCR, self-testing had a sensitivity of 0.71 (95% confidence interval [C.I]) and a specificity of 0.78 (95% C.I). Healthcare professionals and colorimetric readers both performed tests with similar sensitivity and specificity: 0.62 (95% C.I) and 0.67 (95% C.I), respectively; specificity 0.77 (95% CI) and 0.72 (95% CI). An antenatal healthcare professional can read a dipstick for urinary protein with similar accuracy as pregnant women can. In contrast to some previous studies, automated colorimetric testing did not show significant differences. When used in conjunction with self-monitoring in pregnancy, self-testing can play a role in keeping track of one's health.

**Keywords:** Pregnancy, Diagnostic accuracy study, women, hypertension, self-testing.
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## INTRODUCTION

It is well known that dipstick proteinuria analysis is one of the most common prenatalsafeguard tests that is used alongside blood pressure monitoring, to screen for pre-eclampsia [1]. Women at high risk of

pregnancy hypertension typically have their blood pressure checked by midwives at routine antenatal visits [2].

Gestation women should be screened for proteinuria usingan automated colorimetric reagent strip reader with computable confirmation of certain results using a protein or albumin-creatinine ratio according to the (NICE) and (ISSHP) [2,3]. A proteinuria screening tool may not be used regularly with automated readers, however. Approximately 150 obstetricians were surveyed online and found that most of them perform visual tests using dipsticks [4]. Several of the antenatal clinics that are held in primary care practices may not be able to use automated readers because they are expensive and not feasible.

During antenatal care, self-testing could provide more accurate results for detection of preeclampsia [5,6]. Using dipsticks is a popular method for self-testing diabetes because it is inexpensive, convenient, easy to use, does not require any special skills, can provide a quick result, and is easy to use by patients [7, 8]. Despite minimal training and limited experience, it has been found that female are ready and capable of monitoring their avow urine along with their hypertension during pregnancy [6, 9]. There is general positive response to this form of monitoring among pregnant women and healthcare professionals in related qualitative studies [10]. Proteinuria in pregnancy is currently not well studied in terms of its accuracy.

Using aninstance level of laboratory (PCR) quantification, this study compared results of self-testing for proteinuria in pregnant women with chronic or gestational hypertension as well as preeclampsia. Secondly, contrast to the equalinstance of standard, healthcare professionals and automated colorimetric readers were tested for their accuracy. In addition to comparing the accuracy of these index tests with laboratory albumin-creatinine ratios as secondary references, this study had a tertiary objective of determining whether the index tests were accurate.

## METHODS

**Participants**

Pregnant women between the ages of 18 and 50 years who had hypertension (as defined by the International Society for Study of Hypertension in Pregnancy11) or preeclampsia were included in this prospective study.

**Procedure**

Participants were recruited from inpatient wards and antenatal clinics in order to complete the study. In order to participate in this study, women were required to sign a written informed consent form. On the same day that participants were recruited, we gave them a urine sample pot along with a funnel, dipstick tests, and instructions so that they were able to perform protein testing at their bedside as soon as they were recruited, as long as they had access to a clinic. In order to document the results of the urinary proteinuria test, participants filled out a case report form (CRF). A urine sample, masked to the participant's results, was retested using the same dipstick method by a healthcare professional using the same dipstick method. It was determined by an individual from the study team using a dipstick test using an automated colorimetric reader, whether the urine sample was positive or negative for a range of pathogens and then sent to a member of the laboratory team who was blind to the results of the other tests for PCR and ACR testing in the lab. We stored and tested urine samples according to current guidelines in order to minimize the degradation of the samples [12].

**Performance measures and outcomes of the study**

PCR and ACR were compared to dipstick tests in terms of their performance. The dipstick test was considered as the primary index test. While an automated reader and a healthcare professional could also be considered secondary index tests, the dipstick result was considered to be the primary index test. It was decided to use the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios as performance measures following the

guidelines for reporting diagnostic accuracy studies (STARD) [13].

It is also important to note that indexes were also categorised in the following categories when using an automated reader: negative, trace, 1+, 2+, 3+, and 4+, except for those tests which did not use the categorizations negative, trace, 1+, 2+, and 3+. The categories 'positive' and 'negative' were considered to be index test positives, respectively [2, 14]. Test results of PCR within the laboratory that show a value of 30 mg/mmol.

**Power calculation**

Index tests were expected to have sensitivity of 80-90 percent compared to primary index tests [6]. For an estimate of sensitivity in this range with a standard error of no greater than 4% (95% confidence interval), at least 100 complete laboratory-confirmed proteinuria cases would be needed. It was continuously monitored how many cases of laboratory-confirmed proteinuria were recruited and the recruitment process was halted once 55 cases of laboratory-confirmed proteinuria were recorded, in order to provide for possible missing data in the analysis. Our recruitment process was monitored throughout, which allowed us to allow for the possibility of missing data to occur during the recruitment period.

**Statistical analysis**

STATA-14 was used to analyze the data. Baseline characteristics were described using descriptive statistics. In accordance with the thresholds described above, sensitivity, specificity, PPV, and NPV of the index tests were calculated in relation to PCR and ACR as primary and secondary reference tests, respectively. A Receiver Operating Characteristic graph was presented for each dipstick threshold (negative, trace, 1+, 2+, 3+, 4+). All index tests were evaluated based on their likelihood ratios. In the present study, samples without the index test data or with non-existent data for the primary reference test were excluded from the study.

**RESULTS**

The total number of pregnant women who completed the study was 172. One case was excluded from the primary analysis due to a missing healthcare professional visual read result, and four cases were excluded due to a lack of available laboratory PCR results, so 167 (97%) of the cases were not included in the primary analysis. The primary analysis included 6 participants who did not have any results from ACR, but whose ACR results were available.The recruitment of six participants (4%) was found to be unsuitable for inclusion because one of them was of an age that was out of range, and six of them were recruited under the gestational age specified in the inclusion criteria (at 12–19 weeks' gestation). As these protocol deviations were unlikely to result in bias in the study, all 6 were included in the analysis based on the 'intention-to-treat' principle.Among the pregnant women participating in the study, the median age was 32 years, and the median gestational age was 33 weeks at the time of recruitment. Among the 59 women (35%) with proteinuria, 59 were in their first ongoing pregnancy (52%) and had a reference standard (PCR; Table 1) of 30 mg/mmol.There was a sensitivity of 0.61 (95% confidence interval [CI]) and specificity of 0.78 (95% CI) for the self-testing of participants compared to the primary reference test that involved the use of PCR. Compared with the primary reference test, healthcare professionals had a sensitivity of 0.62 (95% CI) and the automated reader had a sensitivity of 0.67 (95% CI), while specificity was 0.77 (95% CI) and 0.72 (95% CI). ACR was used as a secondary reference test for index tests. Similar results were observed (Table 2). An automated reader was found to have a kappa value of 0.50, while self-testing was found to have 0.51, healthcare professionals had 0.51, and PCR demonstrated a value of 0.50 for each index test.Accordingly, a sensitivity analysis was carried out by excluding the six participants recruited in error from the sample, but similar results were obtained (data not shown). In 11 of 17 participants, PCR results were between 30 and 50 mg/mmol, resulting in a false-negative rate of 0.18. For healthcare professionals, the false-negative rate was 0.16, while for automated readers, the false-negative rate was 0.11, with 10 of 16 false-negative results for PCR being within the 30 mg/mmol range and 8 of 13 false-negative results falling

within this range for the automated reader.Receiver-operator characteristic (ROC) plots of the index test. As can be seen from the ROC curves, the index tests exhibit similar sensitivity across a variety of cut-offs.

**Table 1: Demographics value**

| **Studies population demographics** | | |
|---|---|---|
| | **Median** | **IQR** |
| Life span | 32 | 30-36 |
| Pregnancy age at recruitment in weeks | 33 | 28-37 |
| | **Prevalence** | **%** |
| First pregnancy | 86 | 52 |
| Frequency of proteinuria | 59 | 35 |

Abbreviation: IQR, interquartile range.

## DISCUSSION

### Findings of the study

It is comparable to the accuracy of diagnostic tests administered by healthcare professionals to detect proteinuria in pregnant women. ACR (8 mg/mmol) or laboratory PCR (30 mg/mmol) were acceptable as reference standards.A majority of false-negative dipstick results recorded in this study were within the range of 30-50 mg/mmol; however, dipsticks have limitations regardless of who reads them. NICE recommends repeat tests when there are no other signs or symptoms of preeclampsia, or when diagnostic uncertainty remains. The goal is to prevent the diagnosis of pre-eclampsia based on a single raised PCR result due to the variation in protein excretion throughout the day and between days [2]. In previous research, patients with a serum magnesium level of 30 to 50 mg/mmol would benefit from a repeat laboratory test [14,15].



**Table 2:** Performances for both primary and secondary index tests against a primary reference standard

| **Threshold 1 + PCR (protein: Creatinine ratio)** | **Participants (Albustix) *n* = 167** | **Healthcare professionals (Albustix) *n* = 167** | **Automated reader (Clinitek status + Analyser, URISTIX) *n* = 167** |
|---|---|---|---|
| Sensitivity | 0.60 | 0.62 | 0.67 |
| *n*/*N* | 42/59 | 43/59 | 46/59 |
| Specificity | 0.78 | 0.77 | 0.72 |
| *n*/*N* | 96/108 | 95/108 | 90/108 |
| Positive predictive value | 0.66 | 0.65 | 0.61 |
| *n*/*N* | 42/54 | 43/56 | 46/64 |
| Negative predictive value | 0.74 | 0.75 | 0.76 |
| *n*/*N* | 96/113 | 95/111 | 90/103 |
| Positive likelihood ratio | 5.1 | 4.8 | 3.6 |
| Negative likelihood ratio | 0.2 | 0.2 | 0.2 |
| False-positive rate | 0.10 | 0.11 | 0.16 |
| | 12/108 | 13/108 | 17/108 |
| False-negative rate | 0.18 | 0.16 | 0.11 |

| | | | |
|---|---|---|---|
| | 17/59 | 16/59 | 13/59 |
| Kappa value | 0.50 | 0.51 | 0.50 |

Women are asked about their symptoms and their blood pressure is checked, as well as any signs or symptoms of concern are repeated. Urinalysis is not performed in isolation, however: women are also asked about symptoms, and their blood pressure is checked. As this is a screening test that is quantified with a laboratory test, the low proportion of false positives has fewer clinical implications. An antenatal care provider commonly uses dipstick urinalysis because it is inexpensive, convenient, easily repeatable, noninvasive, and noninvasive. Diagnostic screening tests, such as blood glucose monitoring for diabetics, have shown to be more accurate when repeated [16]. To reduce the number of false negative results when self-testing for proteinuria, this would be the case, hypothetically. Increasing sensitivity is likely to be achieved by conducting home self-tests twice a week rather than once a month, thus reducing the possibility of a falsely reassuring negative result [17].

**Limitations and strengths**

The size of the sample in this multi-center study, 167 women, enhanced its power as a diagnostic accuracy study. Most participants (97%) completed the study, and most of the missing results were caused by laboratory errors. According to the authors, this is also the first study to evaluate accuracy in comparison with prenatal women, healthcare professionals, and an automated reader based on two reference tests. In a variety of hospital settings, pregnant women who are generally suitable for self-testing were recruited. There is a high proportion of ethnic minority participants in studies on hypertension and preeclampsia. Another strength of this study was the use of PCR as the primary reference standard. Proteinuria can be quantified using laboratory PCR rather than 24-hour urine collection [8]. Rather than collecting urine 24 hours a day, NICE recommends two PCR tests since they are more accurate, [15] less time-consuming, and more convenient. It has rarely been discussed in point-of-care studies and in PCR studies about self-testing for proteinuria when it comes to point-of-care drug testing for proteinuria [20].

As a result of only having pregnant women undergo one test at a clinic, the study had some limitations. Repeated testing at home may not provide accurate results. As in a remote management regime, study participants were not responsible for deciding what to do after performing self-tests. However, preliminary results demonstrate the feasibility of home self-testing, which should be tested formally in future studies aiming to improve early detection of preeclampsia in pregnant women.

**Interpretation**

According to the results of this study, pregnant women who self-test and healthcare professionals who self-test do not differ clinically. Automated readers did not offer any clinically significant advantages. In comparison with automated readers, visual dipstick urinalysis has shown a relatively low sensitivity (41% compared with 64%) for healthcare professionals. Results reported for studies using an automated reader varied, but consistent sensitivity of 70% was reported for various dipsticks using the reader. In order to reduce observer error and increase sensitivity, NICE and ISSHP recommend using an automated reader 2,3.

This study's results are in line with pilot studies using synthetic urine samples, which revealed similar accuracy and sensitivity and specificity for healthcare professionals and pregnant women (>70%) [6]. This study compared dipstick urinalysis with two previous studies which found a low sensitivity to urinalysis, but the reference test used in two of them was 24-hour urine collection as the reference standard. 24-hour urine collection is less accurate than a PCR test, which may explain why there is a difference between the two studies 15. There may also be population differences underlying discordant findings; for instance, one previous study had a lower prevalence of proteinuria in pregnant women who were non-hypertensive. These differences may also be

explained by interpretation errors; this study used a single test dipstick instead of a multi-test dipstick that had multiple tests to interpret.

Studies have reported findings with high specificity (more than 80%) in this study. In previous studies, no self-testing was included, and visual assessments were performed by study team members or healthcare professionals.

Currently, patients are routinely performed in-clinic urinalysis using a noninvasive method that is easy to repeat, noninvasive, and is often mixed with many other tests in order to gain a complete picture of their health. Dipsticks for urine analysis are cheap and easy to use, so a self-testing regimen incorporating repeat home tests and/or a combination of home and clinic testing could improve early preeclampsia detection. Pregnant women can perform dipstick tests themselves and they provide a rapid result compared with laboratory tests; they are also the most accessible point-of-care test available in pregnancy. Remote antenatal care monitoring has increased during COVID-19's outbreak; [4] repeat self-testing and other self-management activities, including blood pressure self-monitoring, may be effective in high-risk pregnancies. Through the inclusion of more elements of standard antenatal care checks, remote care can increase surveillance and information gathering in between antenatal visits, as well as increase confidence in remote care.

Clinicians and pregnant women seem to be OK with self-testing in a home setting, based on related qualitative research [10]. As a consequence, automated readers are expensive and may not be suitable in all antenatal care settings, even if they are expensive. Visually reading a dipstick is a more accurate method than an automated reader since they are both comparable in accuracy.

## CONCLUSION

Health professionals perform dipstick tests in clinics, but self-testing appears to be an effective alternative. Health professionals may administer dipstick tests in clinics as an alternative to such a regime. It is comparable to current antenatal urinalysis methods, as the tests can be repeated to reduce the possibility of false-negative results.As a result of the current COVID-19 pandemic, it has become more important to find an alternative to in-person care that is safe, effective, and viable. In order to demonstrate that pregnant women can test for proteinuria accurately, researchers should develop a home-based self-testing regime focused on efficiency and accuracy. Self-testing, in conjunction with other self-monitoring activities, must be studied further in the context of health systems to determine whether it is effective without substantially increasing healthcare professionals' workloads. The objective of our study is to perform an evaluation not only of how self-testing can improve health equity and the experiences of women involved in antenatal care, but also how self-testing can contribute to better health equity and women's participation in reproductive health care.



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