Research Article

Validity assessment of self-reported smoking status to detection of urine cotinine levels among patients with tuberculosis undergoing tobacco cessation treatment

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ABSTRACT

Introduction and Aim: Tobacco cessation programs by and large use self-reporting as the gold standard for assessing tobacco use. However, self-reporting may be skewed due to the socio-demographic profile and the context in which the respondents share their tobacco history after undergoing tobacco cessation treatment. It is therefore, imperative to validate the respondents' self-reported smoking status in an effective manner. Hence, this study aimed in validating the self-reported smoking status of study participants with their urine cotinine levels in a randomized controlled trial on smoking cessation.

Materials and Methods: A cross-sectional study was conducted in Dakshina Kannada district of Karnataka to validate the self-reported smoking status of 300 participants. A seven-day point prevalence of smoking status was assessed based on a questionnaire and validated further using the semi-quantitative urine cotinine test at the end of a randomized smoking cessation study.

Results: The sensitivity and specificity of self-reported smoking status was 73.17% and 95.79% respectively. Other validity indicators like positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and accuracy were estimated to be 97.40%, 62.33%, 17.38%, 0.28%, and 80.33% respectively. Cohen's kappa statistics showed a substantial agreement (k=0.61; SE= 0.04) between the two test methods. Educational status and the level of motivation to quit showed a significant association between the test methods.

Conclusion: Self-reported smoking status of participants is not sensitive in identifying smokers thus leading to under-reporting.

Keywords: Validation study; urine; cotinine; biochemical verification; smoking cessation.

INTRODUCTION

In India, nearly one fourth (28.6%) of all adults currently use either smoking or smokeless forms of tobacco (1). The World Health Organization (WHO) recommends integration of tobacco cessation interventions into programs such as tuberculosis (TB) and general health care (2). However, surveillance and monitoring are important for smoking cessation programs since self-reported smoking status may be invalid at times (3) as the respondents' experiences of pressure could be influenced by social and medical disapproval (4). In most studies, standardized questionnaire is a commonly used tool to assess smoking prevalence which has inherent recall and respondent biases (5). To overcome this, specific and sensitive measures of smoking involve testing for cotinine, a metabolite of nicotine present in plasma, saliva, or urine. Cotinine has a half-life of 20 hours allowing its detection in smokers for up to a week after the last smoke. Urinary cotinine test strip is an inexpensive, reliable, and a valid test to measure cotinine levels to assess the smoking status of individuals (6). Cotinine is considered the best indicator of tobacco smoke with a high rate of sensitivity and specificity (7).

Sensitivity of the self-reported tobacco measure has been shown to vary between males and females (83.37% vs 38.6%) and also between age groups of 45-59 years and 60- 69 years (82.27% vs 68.02%) (8). Yet, using biochemical tests as a gold standard cannot be a vital solution to resolve misclassification errors, because sensitivity and specificity the key directories for assessing validity, are in a trade-off relationship (9). In studies comparing questionnaire responses on smoking status with cotinine measurements, the misclassification rates range between 0.9% to 9.8% (10). Hence, in this study we ascertained to determine the validity of self-reported smoking status among tuberculosis patients undergoing nicotine replacement therapy (NRT) for smoking cessation, based on a self-assessment questionnaire and urine cotinine semi-quantitative results.

MATERIALS AND METHODS

Study design and study setting

This cross-sectional validation study was conducted at the end of six months of intervention in a randomized controlled trial among pulmonary tuberculosis patients undergoing nicotine replacement therapy (NRT) for smoking cessation in Dakshina Kannada District of Karnataka State. Only the experimental arm received NRT. The study was conducted between August 2020 to April 2021.

Study population and sampling

The target population was adult pulmonary tuberculosis patients with a current history of tobacco smoking who had registered for Directly Observed Therapy Short Course (DOTS) in Dakshina Kannada District of Karnataka. The participants were from various primary health centres of Mangaluru Taluk. Paediatric TB, mono or Multi-Drug Resistant TB patients, smokeless tobacco users, patients contraindicated for NRT were excluded from the study. The sample size was estimated as minimum 300, based on an earlier described protocol which included 5% cessation in the control group, 15% in the intervention group and an attrition of 20% (11).

Study tools

Two study tools were used in the study - a standardized questionnaire and a urine cotinine cassette test (semi-quantitative, rapid, visual immunoassay for detecting cotinine in human urine with a cut-off point of 200 ng/ml). The questionnaire was used to assess the self-reported smoking status of the respondents ("Yes" or "No") for 7-day point prevalence. The respondents were later requested to provide the urine sample, which was tested with ISO and CE approved urine cotinine rapid test kits [Brand name: Juscheck, Hong Kong]. Discrepancy was defined as a difference in the smoking status between self-reporting and urine cotinine test results (4).

Urine cotinine test

Fresh sample of urine was collected from each of the participant in a sterile container. Three drops of urine were placed onto the specimen well of the cassette using a dropper. Results were interpreted within five minutes of dropping the urine sample into the specimen well. Development of a single red line in the control panel (C) indicated a positive result, interpreted as "smoking non-abstinence". A negative test result corresponded to two red lines one each in the (C) and test (T) panels which was interpreted as "smoking abstinence". A single line in the (T) panel was considered as an invalid test result (Fig1).

Statistical analysis

This study analyses the validity of self-reported smoking status of the participants against biochemically verified urine cotinine test results. True Positive (TP) are those participants who self-report as smokers and also test positive to urine cotinine (i.e., smoking confirmed); True Negative (TN) are those participants who self-report as non-smokers and also test negative to urine cotinine; False Positive (FP) are the participants who self-report as smokers but test negative to urine cotinine; False Negative (FN) are the participants who self-report as non-smokers and then test positive to smoking with urine cotinine. Misclassifications were calculated by under-reporting and over-reporting. Under-reporting rate was defined as the percentage of self-reported current non-smokers who were bio verified as active smokers. Over-reporting rate was defined as the percentage of self-reported current smokers who were bio-verified as non-smokers.

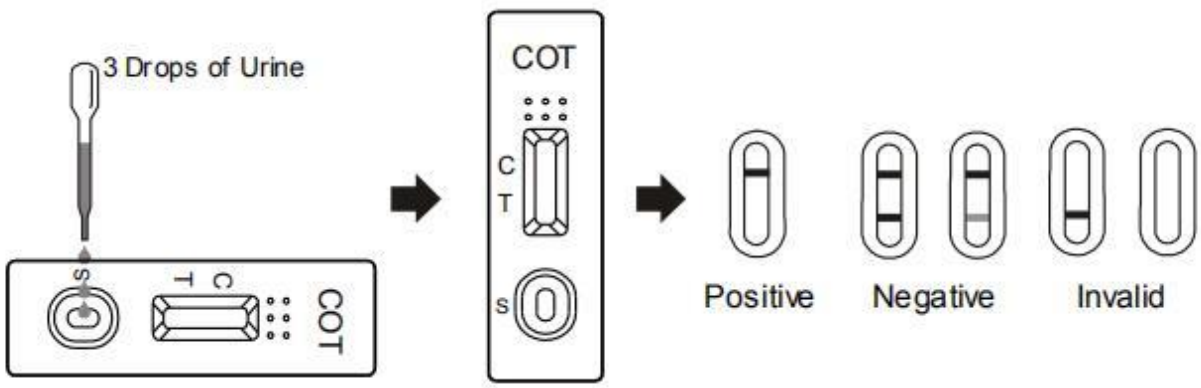

Fig 1: Interpretation of urine cotinine test results for tobacco use

All relevant data obtained were subjected to descriptive analysis first, and the results reported as number and percentage. Cohens' Kappa statistic was used in determining the agreement between self-reporting and urine cotinine testing results. Sensitivity, specificity, likelihood ratios and predictive values, and other validity indicators were determined at 95% confidence interval (CI) using Medcalc statistical software. Chi square test was used to determine the association between the test methods and trial arms. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) (https://www.ibm.com/in-en/products/spss-statistics).

Ethical considerations

Approval was obtained from the Institutional Central Ethics Committee, Nitte (Deemed to be University), (NU/CEC/2019/209 dated 30th January 2019). The study is registered with the Clinical Trials Registry of India (CTRI/2018/11/016457 dated 1.12.2018). Administrative approval was obtained from the appropriate authority at the district level. Participant information sheet was narrated orally and written informed consent was obtained prior to the recruitment of participants. Identity of the participants was anonymized.

RESULTS

In the study, out of 300 participants, biochemically verified non-smokers and smokers were 95 (31.66%) and 205 (68.34%) respectively. Of the 205 biochemically verified smokers, 150 (73.17%) self-reported as smokers. Similarly, of the 95 biochemically verified non-smokers, 91 (95.78%) self-reported as non-smokers. There was a significant difference between the test results of the urine cotinine and self-reported smoking status ($p<0.05$) as shown in Table 1.

The self-reported smoking status of the participants when biochemically verified with urine cotinine test, the sensitivity and specificity of the self-report were 73.17% and 95.79% respectively. The positive predictive value and negative predictive values were 97.40% and 62.33% respectively (Table 1). The positive likelihood ratio and negative likelihood ratio were estimated as 17.38 and 0.28 respectively. The accuracy of the test was 80.33% (classification error: 19.67%). Cohen's kappa value and Mathew's correlation coefficient were 0.61 and 0.64 respectively. The F1 score for the study was 83.57% (Table 2).

Table 1: Validation of self-reported smoking status with urine cotinine rapid test

	Urine cotinine test positive (smoker)	**Urine cotinine test negative (non-smoker)**	**Total**	**Chi square statistic**	**p value**
Self-reported smoker	150 (73.17%)	04 (4.22%)	154	123.57	< 0.01
Self-reported nonsmoker	55 (26.83%)	91 (95.78%)	146		
Total	205 (100%)	95 (100%)	300		

Table 2: Validity and clinical relevance of self-reported smoking of study participants

Validity parameters	**Value**	**95% CI**
Sensitivity	73.17%	66.55%- 79.10%
Specificity	95.79%	89.57%- 98.84%
Positive predictive value	97.40%	93.47- 98.99%
Negative predictive value	62.33%	56.80%- 67.56%
Positive Likelihood Ratio	17.38	6.64- 45.51
Negative Likelihood Ratio	0.28	0.22- 0.35
Accuracy	80.33%	75.38%- 84.68%
Classification error	19.67%	15.56- 24.54%
Cohen's kappa	0.61	SE 0.04 (0.51- 0.68)
Mathew's correlation coefficient	0.64	0.56- 0.70
F1 score	83.57%	78.34- 86.83%

Age groups of the participants were associated with self-reported smoking status and its biochemical verification. Majority of the participants were aged between 31 and 60 years who self-reported smoking which was also verified biochemically. There was no significant difference between age groups and the test methods used ($p>0.05$). Gender wise males dominated the list with a self-reported smoking status of 94.80% and a verified urine cotinine smoking status of 95.60% (Table 3). There was no significant difference between gender and the test methods used ($p> 0.05$). Majority of the participants who self-reported smoking status were in the preparation stage of trans-theoretical model (49.36%). When verified biochemically, it was reduced to 37.56%. There was a significant difference between the stages of trans-theoretical model and the test method of smoking status ($p<0.05$). Majority of the participants who self-reported smoking had a low dependence to nicotine (90.26%) according to the Fagerstorm score for nicotine dependence. When biochemically verified with urine cotinine results, 93.17% of the respondents had self-reported as having low dependence to nicotine. However, there was no significant difference between the level of nicotine dependence and test methods used ($p>0.05$).

In the experimental arm, the self-reported and biochemically verified smoking status was 48.29% and 44.16% respectively. Self-reported and biochemically verified smoking status in the control arm was 51.71% and 55.84% respectively. There was no significant difference ($p>0.05$) between the intervention arms and the test methods used to measure the smoking status (Table 3).

Table 3: Association between socio-demographic characteristics, smoking characteristics and test methods

Sociodemographic/ smoking characteristics	**Self-reported smoking (n= 154)**	**Urine cotinine verified smoking (n= 205)**	**Chi-square statistic**	**P value**
Age (in years)				
30 and below	13 (8.44%)	20 (9.75%)	1.04	0.79
31- 45	65 (42.20%)	81 (39.51%)		
46- 60	61 (39.61%)	78 (38.05%)		
> 60	15 (9.75%)	26 (12.69%)		
Gender				
Male	146 (94.80%)	196 (95.60%)	0.12	0.72
Female	08 (5.20%)	09 (4.40%)		
Occupation				
Professional/clerical	46 (29.87%)	66 (32.20%)	0.22	0.89
Skilled/unskilled labour	80 (51.95%)	103 (50.24%)		
Unemployed	28 (18.18%)	36 (17.56%)		
Education				
Illiterate	35 (22.73%)	79 (38.54%)	10.21	0.006*
School education	107 (69.48%)	112 (54.63%)		
College education	12 (7.79%)	14 (6.83%)		
Stage of Transtheoritical model				
Precontemplation	05 (3.24%)	05 (2.44%)	10.94	0.02*
Contemplation	30 (19.48%)	31 (15.12%)		
Preparation	76 (49.36%)	77 (37.56%)		
Action	24 (15.58%)	55 (26.83%)		
Maintenance	19 (12.34%)	37 (18.05%)		
Fagerstrom score for nicotine dependence				
Low dependence	139 (90.26%)	191 (93.17%)	1.01	0.31
Moderate to high dependence	15 (9.74%)	14 (6.83%)		
Intervention arm				
Experimental	99 (48.29%)	68 (44.16%)	0.60	0.43
Control	106 (51.71%)	86 (55.84%)		

*Statistically significant $p < 0.05$

DISCUSSION

Validation of self-reported smoking status with cotinine in low- and middle-income countries is limited. Given the widespread use of self-report data in smoking cessation programs, it is deemed important to assess the accuracy of such reports (7). In this study, we assessed the accuracy of self-report of smoking status in tuberculosis patients at the end of a randomized controlled trial on smoking cessation among TB patients in Mangaluru. Biochemically verified smokers outnumbered self-reported smokers (68.33% vs 51.33%) with a significant difference in our study. A study conducted among adults in Georgia, USA, showed cotinine detected smoking significantly outnumbering self-reported smoking (32.27% Vs 26.44%). This suggests that self-reported measures of smoking status may lead to an under-estimation of smoking prevalence (8).

Our study had 150 (50%) true positives and 91 true negatives (30.33%). False positives and false negatives were 4.22% and 26.83% respectively. The vital part of this study is to identify the false negatives who report smoking abstinence and eventually test positive biochemically. There is a significant difference between the two test methods and the smoking status of the participants ($p < 0.05$). These results were in line with a study conducted in two medical centres of USA among head and neck cancer patients that showed a significantly high proportion of false negatives (24%) after adjusting for other nicotine sources (12).

The sensitivity and specificity of the smoking questionnaire in this study was 73.17% and 95.79% respectively. A study conducted in Korea among firefighters showed a sensitivity and specificity of self-reported smoking status at 42.98% and 99.08%, respectively (3). The Canadian Health Measures Survey demonstrated a high sensitivity and specificity of 91.6% and 98.3% respectively (13). A study on Korean adolescents revealed a low sensitivity and high specificity of 67.4% and 97.9% respectively (9). This shows that self-reporting of smoking status varies across populations and regions based on the context in which they are studied. The self-report is valid only when verified with biomarkers for identifying misclassification. Our study shows a misclassification among 59 participants (19.67%) thus reflecting an accuracy of 80.33%. Misclassification rate of self-reported cigarette smoking through serum cotinine verification among light smoking adult survivors of childhood cancer in St. Jude Lifetime Cohort Study was 14.3%(14). Under-reporting may be due to self-reporting as current smoker although abstinent for more than seven days prior to the bio verification. The positive predictive and negative predictive values in the study are 97.40% and 62.33% respectively. A lung cancer screening trial showed a higher positive predictive value of self-reported smoking of 97%, and comparatively lower negative predictive value of 87%(6).This indicates that self-reporting of smoking status is less effective in confirming the true negatives among the self-reported non-smokers while, it is easier to confirm the true positives among all the self-reported current smokers. This finding is realistic as rarely a non-smoker reports as a smoker while the reverse is a common phenomenon. This also impacts the positive and negative likelihood ratio of self-reporting which are 17.38 and 0.28 respectively. A Mexican study conducted on adolescents revealed a positive likelihood ratio of 5.1, which is moderate in probability. This difference may be due to the differing populations and its effect on contextual social disapproval of smoking(6).This reassures that self-reporting of smoking status has a greater ability to identify the smokers but ineffective in identifying the non-smokers. The overall agreement between self-reported smoking status and urine cotinine test was 0.61 which could be interpreted as having substantial agreement as per Cohen's kappa statistic. A study in Malaysia involving adolescents also showed a substantial agreement but with a higher kappa value of 0.75(4).The Mathew's correlation coefficient (MCC) in our study was 0.64 which is interpreted as "better than random, but not perfect prediction". No studies have analysed for MCC in a context similar to our study. MCC provides a high-quality score both on the majority of the negative and positive cases, independently of their ratios in overall dataset (15).The F1 score is 0.83 which is considered reasonable when compared to the ideal best value of 1.0. However, no studies showed F1 scores in a similar context for comparison.

When assessed for an association of sociodemographic and smoking characteristics with the method of smoking confirmation, there was a significant difference between level of education and the test method used ($p<0.05$). Illiterate respondents were more likely to under-report smoking (22.73%) when compared to 38.54% with bio- verification. However, the number of respondents did not differ much between the two tests for school education, and college education. This result was in line with pregnant women in the second trimester in China who under-reported their smoking status when compared to urine cotinine test (82.98% vs 98.58%) if they had less than six years of formal education ($p<0.05$) (16). According to the stage of motivation based on the trans-theoritical model of behaviour change, respondents under-reported their smoking status when they claimed to be in the action and maintenance phase which showed a significant difference with bio verification ($p<0.05$). The respondents may have falsely claimed as having quit tobacco despite their continued use. However, no

studies were found to compare the results. The Fagerstrom scale was used to know the level of nicotine dependence among the respondents. We found that respondents with low dependence marginally under-reported smoking status when bio-verified (90.26% vs 93.17%) to be not statistically significant (p>0.05).A study conducted in Gujarat showed a weak correlation (r = 0.081) of salivary cotinine with FTND score which indicates that salivary cotinine level is weakly influenced by psychological dependence (17). The study over-reported smoking status in the experimental arm that underwent nicotine replacement therapy (48.29% vs 44.16%) and vice versa in the control arm that took only brief advice with mint chewing gums as a placebo (51.71% vs 55.84%). There was no significant association between the interventions and the test methods. These results are similar to a study conducted in multi-site randomized clinical trials conducted between 2010 and 2014 in hospitals across the United States, wherein the verified abstinence for the intervention and control arm with saliva cotinine method was 57.6% and 58.0% respectively which did not show significant difference (18). To the extent of our knowledge, this study is unique as there are limited studies conducted in India to validate self-reported smoking with cotinine test, especially among tuberculosis patients in government healthcare settings.

CONCLUSION

The study was able to identify the significance of biochemical verification of smoking status of the study participants. Self-reported smoking in smoking cessation programs is not effective due to an overwhelming under-reporting of smoking status which negatively impacts scientific research. Hence, biochemical verification of self-reported smoking is essential in tobacco cessation research and clinical practice.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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