Comparative Analysis of Urine Microalbumin Levels in Traditional and Nicotine-Containing Electronic Cigarette Smokers

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ABSTRACT

The usage of electronic cigarettes, or "e-cigarette," as a substitute for traditional cigarettes has skyrocketed since their introduction, particularly among teenagers and young adults. However, there is still a dearth of knowledge on the usage of e-cigarettes and renal health. This study compared the levels of urine microalbumin, an indicator of kidney damage, in smokers who use traditional cigarettes versus those who use e-cigarettes that contain nicotine. Urine samples were taken for the study from both groups, and the microalbumin levels were determined using the dipstick method. Based on the result, the mean microalbumin for traditional smokers (TS) was 27.1 mg/L, while for e-cigarette smoker (ES) was 28.5 mg/L – with non-smokers (NS) as negative control group, having mean of 14 mg/L. Both groups significantly differed from the negative control group ($p \leq 0.001$), but there was no significant difference in microalbumin levels between traditional cigarette users and nicotine-containing e-cigarette users ($p = 0.854$). Findings revealed that the urine microalbumin levels in nicotine-containing e-cigarette users are comparable to those in traditional cigarette smokers, indicating similar levels of renal damage in both groups. This imply that, in contrast to what is commonly believed, e-cigarettes and traditional cigarettes both provide similar risk to kidney health.

Keywords: E-Cigarette, Microalbumin, Nicotine, Traditional Cigarettes

INTRODUCTION

The pernicious health impacts of smoking are extensive, making it the most significant modifiable risk factor for reducing overall morbidity and mortality (Yusuf et al., 2020). Each year, tobacco-related diseases cause 8 million deaths globally, with an estimated 1.3 million of these fatalities occurring among non-smokers (NS) exposed to second-hand smoke (World Health Organization, 2023). In the Philippines, the Lung Center of the Philippines reports that an average of 321 people die daily from tobacco-related illnesses (Philippine News Agency, 2022).

With several health issues linked to traditional smoking, electronic cigarettes, or "e-cigarettes," have been proposed as a safer alternative (Marques et al., 2021). Since then, e-cigarette use has dramatically increased, especially among adolescents and young adults (Famiglietti et al., 2021). The growing acceptance of e-cigarettes is seen as crucial for public

health. However, despite substantial evidence linking traditional smoking to kidney damage, little is known about the broader health effects of e-cigarettes. This is partly due to their status as a relatively new product and the focus of most research in this area on respiratory issues (Jha et al., 2021). This study aims to explore the connection between e-cigarettes and kidney health, specifically their role in the development of microalbuminuria, by comparing microalbumin levels among traditional smokers (TS) and e-cigarette smokers (ES) in the Philippines.

LITERATURE REVIEW

This literature review provides information relevant to the variables involved in this study, namely microalbumin, traditional smoking which includes nicotine consumption, electronic cigarette use, and non-smoking. Furthermore, this portion delves into the discussion of the relationship between nicotine-containing electronic cigarettes and microalbumin levels.

Microalbumin

The occurrence of microalbumin in the urine often referred to as "microalbuminuria" indicates an anomaly with the glomerular filtration barrier (Márquez et al., 2019; Budhathoki-Uprety et al., 2019). Microalbuminuria in the glomerular basement membrane (GBM) results from several mechanisms. The poroelastic model indicates that podocyte foot process loss leads to GBM expansion, enlarging pores and increasing albumin leakage. Along with slit diaphragm constriction, this contributes to reduced filtration and GBM thickening observed in albuminuria (Aypek et al., 2022; Xu et al., 2023). Such damage increases endothelial permeability in various blood vessels, which promotes arteriosclerosis. This, in turn, helps explain the heightened risk of developing cardiovascular disease and retinopathy (Martinez et al., 2022).

Microalbuminuria is the earliest marker of kidney disease and elevated cardiovascular risk (Martinez et al., 2022). Research by Gupta et al. (2014) found that non-diabetic, normotensive smokers have significantly higher levels of urinary albumin and urinary albumin-to-creatinine ratio (ACR) compared to non-smokers, with these levels increasing in proportion to the amount of smoking. Smokers also experience a fourfold higher prevalence of microalbuminuria and a 16-fold higher prevalence of elevated urinary ACR relative to non-smokers. While smoking significantly reduces HDL levels, it does not appear to affect serum creatinine or creatinine clearance significantly. According to Eid et al. (2022), smoking is an independent risk factor for the accelerated progression of chronic kidney disease (CKD) in nephritis cases. Given that urinary albumin is a well-established marker of glomerular damage, the association between smoking and albuminuria indicates that smoking may cause direct or indirect harm to the kidneys.

Traditional Smokers

Tobacco smoking is a leading cause of preventable disease and death globally (Le Foll et al., 2022). Tobacco smoke contains numerous carcinogens and harmful chemicals, including its key component, the addictive compound nicotine (Benowitz et al., 2016; West, 2017). Nicotine, a highly addictive alkaloid with strong parasympathomimetic effects, is derived from the dried stems and leaves of Nicotiana tabacum (Alkam et al., 2019). Each cigarette typically contains 8–20 mg of nicotine, with an average of 12 mg (Calvo-Flores et al., 2018). Smoking

delivers nicotine quickly and efficiently to the brain, making it accessible, cost-effective, and highly addictive (West & Shiffman, 2016).

Smoking significantly increases the risk of chronic kidney disease (CKD) (Choi et al., 2019). Research shows a clear link between longer smoking duration and a higher risk of CKD progression, particularly in patients with an estimated glomerular filtration rate (eGFR) below 45 ml/min/1.73 m² and proteinuria under 1.0 g/g. While the available literature does not specify how long people smoked before developing proteinuria, study participants generally have a long history of smoking (Wu et al., 2021). Nicotine plays a critical role in the development of renal disease by causing oxidative stress, renal fibrosis, increased mesangial proliferation, and extracellular matrix deposition. Recent studies indicate that nicotine reduces cell viability and promotes reactive oxygen species (ROS) production in human kidney cells, directly contributing to oxidative stress and activating pathways related to fibrosis and cell death (Zheng et al., 2020; Raja et al., 2022). It also amplifies angiotensin II-induced increases in endothelin while reducing cytoprotective heme oxygenase responses, leading to renal and cardiac damage (Chandrashekar et al., 2019).

Nicotine-Containing Electronic Cigarette Smokers

Electronic cigarettes (e-cigarettes) are battery-powered devices that heat and aerosolize a liquid solution typically containing nicotine, flavorings, and other substances (Baldassarri, 2020; Kathuria, 2022; Chakma et al., 2019). The nicotine content, which is also the main addictive component in tobacco, varies across commercially available e-liquids, and nicotine-free options are also available (Marques et al., 2021). However, teens using e-cigarettes with higher nicotine levels may develop a tolerance to and dependence on nicotine, increasing their risk of continued vaping and potentially transitioning to combustible tobacco products (Goldenson et al., 2017).

Research indicates that both traditional and electronic cigarette smoking can negatively impact renal health, with studies showing an association between smoking and increased albuminuria, particularly among e-cigarette users. However, the reasons for the significantly higher albumin levels in electronic cigarette smokers compared to tobacco smokers are still unclear (Podzolkov et al., 2020). Both types of smoking elevate inflammatory markers, oxidative stress, and cause histological damage in the urinary bladder, though these effects are more pronounced with traditional cigarettes (Abdelwahab et al., 2023). These findings suggest that nicotine exposure from e-cigarettes can lead to microalbuminuria and other renal complications, though the severity may be less than that caused by traditional cigarettes. However, comparative knowledge of urine microalbumin levels between traditional and e-cigarette smokers remains limited.

METHODS

To investigate the effects of traditional and nicotine-containing electronic cigarettes on microalbumin levels, a quantitative study was conducted with 45 participants aged 18-42. The sample included 15 non-smokers (NS) as the control group, 15 traditional cigarette smokers (TS), and 15 e-cigarette users (CS), all selected through purposive sampling. Collaborating

with the local health center in Barangay Puting Kahoy, Silang, Cavite, the study targeted smokers who had used their respective products for at least one year. Participants included those who switched from traditional to electronic cigarettes or vice versa, and those with smoking-related diseases. Experimental groups were categorized based on their smoking history, with those smoking for at least a year placed in their respective categories.

Each sample group received a consent form explaining the study's nature and procedures, and the experimental group completed a pre-evaluation questionnaire adapted from Farsalinos et al. (2014) to assess their smoking device usage, smoking duration, and frequency. Participants were informed about their right to withdraw, which would result in their data and urine analysis results being excluded from the study. Before sample collection, participants were instructed to maintain proper hydration, avoid recent exercise and high-protein diets, and ensure they understood and consented to the test. Urine containers were distributed for participants to fill halfway, label with their names, and return. A single random urine sample from each participant was collected and stored in a portable ice chest to maintain sample quality.

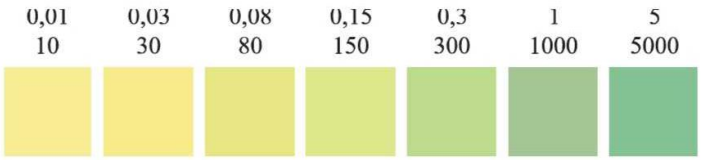

Figure 1. **Color Analysis for Urine Strip Reaction**
Source: PHAN Catalogue of Test Strips for Urine Analysis

After collecting specimens from all participants, microalbuminuria was tested using the Erba Manheim MicroalbuPHAN® urine dipstick method. Figure 2 illustrates the color analysis of microalbumin levels after the strip pads were submerged in urine for one to two seconds. The values in the upper corner of the color reactions represent g/L and mg/L, respectively. Although the strip can also measure the urine albumin ratio (uACR), this study focused solely on urine microalbumin concentrations. The ratio was only obtained to check the increased result of microalbumin among the negative controls. The result was read after one minute by comparing the color change from the strip to the grading values indicated on the body of the strip container, with value gradings of 10 mg/L, 30 mg/L, 80 mg/L, 150 mg/L, 300 mg/L, 1000 mg/L, and 5000 mg/L. According to the manufacturer's interpretation guidelines, albumin typically appears in urine at concentrations below 20 mg/L (0.02 g/L). When concentrations range from 20 to 300 mg/L (0.02 to 0.3 g/L), it is classified as microalbuminuria.

The data recorded were sent to a statistician for treatment and interpretation. The use of mean, median, and standard deviation was used to show the descriptive statistics for the microalbumin levels in each smoking status group. Dwass-Steel-Critchlow-Fligner pairwise comparisons were performed to identify which groups differ from each other.

RESULTS AND DISCUSSION

Microalbumin Levels in Urine of Non-Smoking Participants

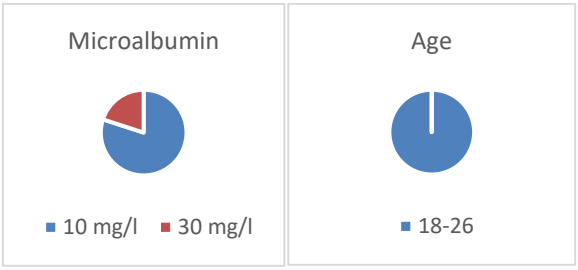

Figure 2. **Microalbumin Levels and Demographics of Non-Smokers**
Source: Authors

Figure 2 presents the microalbumin levels and age range of NS participants, mostly third-year college students aged 18-26, who had normal microalbumin results, with only three initially showing positive tests. After adjusting with the urine albumin-to-creatinine ratio (uACR), these three were confirmed to have normal results, indicating that all NS participants were valid negative controls. Research highlights that non-smokers generally have better renal health compared to smokers. Smoking is linked to increased blood urea, serum creatinine, and urinary albumin levels, along with a decreased estimated glomerular filtration rate (eGFR) (Eid et al., 2022). Studies also show smokers have significantly higher microalbumin levels, up to four times greater than non-smokers (Jha et al., 2021), which persists even after adjusting for confounding factors such as blood pressure and diabetes (Barbato et al., 2019). These findings emphasize the importance of smoking cessation and avoiding secondhand smoke to maintain optimal kidney function and prevent chronic kidney disease (CKD).

Microalbumin Level in Urine of Traditional Cigarette Smokers

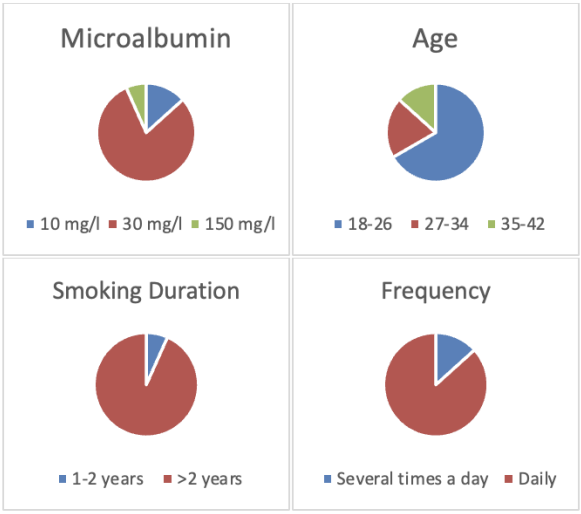

Figure 3. **Microalbumin Levels and Demographics of Traditional Smokers**
Source: Authors

Data on TS, shown in Figure 3, reveal that most had microalbumin levels of 30 mg/L, indicative of microalbuminuria, while two individuals had normal levels (10 mg/L) and one had a higher level (150 mg/L). Results clustered around 30 mg/L across various age groups (18-26, 27-34, 35-42). Participants who had smoked for over two years generally had higher microalbumin levels, whereas a participant with a shorter smoking duration and less frequent use maintained normal levels. The elevated microalbumin level of the individual with the highest reading, despite less frequent smoking, highlights nicotine's adverse impact on renal health, correlating with cumulative smoking exposure as noted by Gupta et al. (2014). Multiple studies have found significantly elevated urinary albumin levels in both active and passive smokers. Smoking is associated with increased arterial stiffness, which may contribute to renal damage (Eid et al., 2022; Podzolkov et al., 2020). Traditional cigarette smokers often exhibit elevated microalbumin levels in their urine compared to non-smokers. (Gupta et al., 2014).

Microalbumin Level in Urine of Nicotine-containing Electronic Cigarette Users

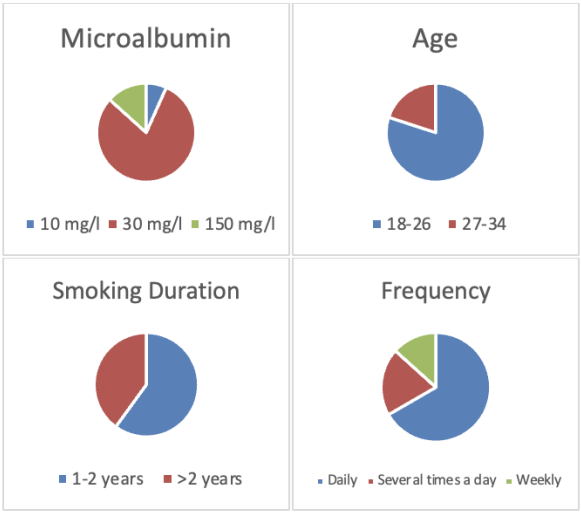

Figure 3. **Microalbumin Levels and Demographics of Traditional Smokers**
Source: Authors

Figure 3 shows microalbumin levels (mg/L), age, smoking duration, and frequency for 15 ES. Most had microalbumin levels of 30 mg/L, indicating microalbuminuria, with two users showing significantly higher levels of 150 mg/L, suggesting greater kidney damage, and one user at a normal level of 10 mg/L. Users aged 18–34, and those who had smoked for one to two years or more, typically had levels of 30 mg/L, with exceptions at 150 mg/L and 10 mg/L. Daily users mostly had 30 mg/L, except one at 150 mg/L. These results suggest potential early kidney damage in ES, with higher levels indicating possible severe impairment. According to Siegel et al. (2020), there is variability in how nicotine is metabolized by the body; compared

to slow metabolizers, fast metabolizers show greater indications of nicotine dependency and remove nicotine more quickly.

Levels of Urine Microalbumin among Traditional Cigarette smokers, Non-smokers, and Electronic Cigarette users

Table 1

Levels of Urine Microalbumin among Traditional Cigarette smokers, Non-smokers, and Electronic Cigarette users

Smoking Status	N	Mean	Median	SD	Min	Max
Cigarette-users	14	27.1	30	7.26	10	30
Non-smokers	15	14	10	8.8	0	30
Electronic Cigarette-users	13	28.5	30	5.55	10	30

Source: Calculated by Authors' Statistician

Table 1 displayed the descriptive statistics for microalbumin levels across different smoking status groups, each consisting of 15 participants (N). To minimize data variability, outliers were removed from the dataset, resulting in differing participant numbers between cigarette and e-cigarette users. The mean microalbumin levels were 27.1 mg/L for cigarette users, 14 mg/L for non-smokers, and 28.5 mg/L for e-cigarette users. Both cigarette and e-cigarette users had nearly equivalent mean levels, with e-cigarette users showing the highest mean. In contrast, the median microalbumin levels were 30 mg/L for both cigarette and e-cigarette users, compared to 10 mg/L for non-smokers. Standard deviations indicated the highest variability among non-smokers (SD = 8.8), followed by cigarette users (SD = 7.26), and the lowest variability among e-cigarette users (SD = 5.55).

The results correlate with a study by Choi et al. (2021), which used a semiquantitative dipstick method and found elevated albumin levels in the urine of smokers. Similarly, Podzolkov et al. (2020) employed the urine dipstick method to measure albumin levels in both traditional and e-cigarette smokers, also demonstrating elevated levels, with e-cigarette users showing the highest mean. These findings support the results of this study and are consistent with prior research on the association between smoking and albuminuria.

Comparison of Microalbumin Levels of Each Smoking Status

Table 2

Dwass-Steel-Critchlow-Fligner for Pairwise Comparisons

Comparison	p-value	Interpretation
Cigarette-user vs. Non-smoker	0.001	Significant
Cigarette-user vs. Vape-user	0.854	Not significant
Non-smoker vs. Vape-user	<0.001	Significant

Source: Calculated by Authors' Statistician

The p-value, which is statistically significant if below 0.005, indicates the level of evidence. The Dwass-Steel-Critchlow-Fligner pairwise comparisons in table 2 revealed that non-smokers had significantly lower microalbumin levels compared to both cigarette ($p = 0.001$) and e-cigarette users ($p < 0.001$). This finding supports Barbato et al. (2019), who showed that active smokers have a higher risk of elevated microalbumin levels compared to non-smokers. However, there was no significant difference in microalbumin levels between cigarette and e-cigarette users ($p = 0.854$), underscoring that both smoking types adversely affect renal health. E-cigarettes, often seen as a safer option, can still cause renal damage. Both traditional and electronic cigarette smoking are associated with increased albuminuria and arterial stiffness in young adults (Podzolkov et al., 2020). E-cigarette aerosols contain toxic compounds that may contribute to renal toxicity through oxidative stress (Raja et al., 2022). These results indicate that both cigarette and e-cigarette use negatively impact renal health, with e-cigarettes also posing risks despite their perceived safety.

CONCLUSION, IMPLICATION, SUGGESTION, AND LIMITATIONS

The study demonstrated that non-smokers had significantly lower microalbumin levels compared to both cigarette and electronic cigarette users, indicating that smoking and vaping have a detrimental effect on kidney function. Although e-cigarette users exhibited higher mean microalbumin levels than cigarette users, the difference was not statistically significant, suggesting that both smoking methods pose similar risks. These findings highlight the need for public health strategies and policies to address the harmful effects of both traditional cigarette and e-cigarette smoking by promoting smoking cessation programs, raising awareness about the risks of kidney damage from smoking and vaping, routine microalbumin screenings for smokers and vapers during check-ups and enforcing stricter regulations on vaping, especially for youth.

Future researchers should consider other lifestyle factors, such as alcohol intake and diet, to better isolate the specific effects of smoking on renal function. Expanding the sample size and studying additional variables like age, length of usage, and frequency can enhance the generalizability of the findings. It is also recommended to adopt stricter participant selection criteria, focusing only on traditional cigarette smokers and e-cigarette users without pre-existing smoking-related diseases, to improve the accuracy in identifying the duration and method of smoking that increases the risk of albuminuria. For testing, using a first-morning urine sample is suggested as it provides the most accurate measure of albumin in urine. While the 24-hour urine protein test is the gold standard for assessing proteinuria, it has limitations, so the spot urine albumin-to-creatinine ratio (ACR) or protein-to-creatinine ratio (PCR) is recommended as a practical alternative (Harrison & Tonelli, 2023, Prasad et al., 2024). Additionally, standardized guidelines for hydration before sample collection should be implemented to ensure consistency in results.

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