

JURNAL KEDOKTERAN

MEDIA INFORMASI ILMU KEDOKTERAN DAN KESEHATAN ISSN 2460-9749 e-ISSN 2620-2890

ISSN 2460-9749

Home: https://jk.unizar.ac.id/kedokteran

Identification of Urine Cotinine in Secondhand Smoke and its Association with Socio-Environmental

Oktadio Erikardo^{*}, Euis Purbasari, Nurul Azmah Nikmatullah

Faculty of Pharmacy and Science, Universitas Muhammadiyah Prof.DR.HAMKA, Jakarta, Indonesia

Article Info

Article History:

Received: Sept 18, 2023 Accepted: Nov 04, 2023 Published: Jun 25, 2024

Corresponding Author:

Oktadio Erikardo oktadioerikardo@uhamka.ac.id

DOI:

10.36679/kedokteran.v9i2.91

 \bigcirc 2024 The Authors. This is an open-access article under the <u>CC</u> <u>BY-NC</u> license.



ABSTRACT

Background: Exposure to cigarette smoke not only affects active smokers but also endangers passive smokers, leading to various health problems. However, research on passive smokers is still very limited, particularly regarding the relationship with socio-environmental factors. Cotinine is the primary metabolite of nicotine consumption and can serve as a biomarker for tobacco use and its derivatives; moreover, its presence is associated with poor health risks. Socioenvironmental conditions are influential factors in smoking behavior, but the relationship between these factors and cotinine identification in passive smokers has not been fully studied. This study aimed to identify cotinine in passive smokers and their relationship with socio-environmental conditions. Methods: This study utilized an analytical survey with a cross-sectional approach. The sample size consisted of 53 passive smokers who had never actively smoked and were over 15 years old. Urine cotinine was identified using a competitive immunochromatography method, and profile of passive smokers was obtained through questionnaires. The collected data were then statistically analyzed. Results: The results showed that 36 samples tested positive for cotinine (67.90%), with the majority being females (28 individuals; 77.80%). Statistical tests indicated a significant relationship between urine cotinine identification and exposure location (p<0.001) and exposure frequency (p<0.001). In contrast, factors such as sex (p=0.570) and occupation (p=0.861) did not show a significant relationship with the identification of cotinine in passive smoker's urine. Conclusion: Factors such as exposure location and exposure frequency are related to cotinine identification, whereas sex and occupation are not related to cotinine identification in passive smoker's urine.

Keywords: Cotinine, Nicotine, Passive Smokers

INTRODUCTION

Cigarette consumption not only endangers the health of active smokers but also individuals around them (passive smokers) through secondhand smoke exposure. However, various information and research predominantly emphasize and focus on the health of active smokers rather than passive smokers. This condition has resulted in a scarcity of data available for comprehensively assessing the impact on passive smokers, including from socio-environmental factors. Various socio-environmental conditions such as the lack of public attention to the enforcement of smoking bans and awareness of the adverse effects of secondhand smoke can increase the risk of secondhand smoke exposure for passive smokers (Sandhi, 2019; Tarigan & Yulianti, 2019).

Cigarette smoke contains about 4.000 chemical compounds, some of which include Polycyclic Aromatic Hydrocarbons (PAHs), Carbon Monoxide (CO), Tar, and Nicotine (Subagya, 2023). Smoke exhaled into the

surrounding environment by smokers contains nicotine levels 4-6 times higher than the smoke that enters the smoker's body (Said & Muluki, 2022; Tanuwihardja & Susanto, 2012). Cigarette smoke also leaves residues (nicotine and various other substances) that are hazardous and can "cling" to surrounding objects such as tables, carpets, and other surfaces (Amalia, 2021). According to Riskesdas data, the prevalence of smoking in the population aged 10–18 years increased from 7.2% in 2013 to 9.1% in 2018 (RISKESDAS, 2019). The increase in the number of active smokers will be accompanied by an increase in passive smokers or secondhand smoke. It is estimated that one-third of the world's population has already become passive smokers (Amelia et al., 2023; Munawaroh et al., 2021).

Individuals exposed to cigarette smoke are at risk of developing diseases resulting from cigarette smoke such as lung damage, heart disease, sore throat, and coughing. Nicotine is the main component found in tobacco cigarette smoke. When smoking, nicotine quickly enters the bloodstream and is metabolized within the body (Lathifah et al., 2020; Oktaviyanti et al., 2023).

The primary metabolite of nicotine is cotinine, which is easily detected in various body fluids such as blood, urine, and saliva (Pujiono et al., 2022). Nicotine metabolism into cotinine occurs in the liver by the cytochrome P450 system (CYP2A6 and CYP2B6), which converts 80% of nicotine into cotinine. The nicotine metabolism process also occurs in the lungs, where nicotine is converted into cotinine (80%) and nicotine oxide (4-7%). The remaining nicotine in the blood is also filtered by the kidneys and excreted through urine (Lathifah et al., 2020; Tzatzarakis et al., 2011).

Cotinine serves as the primary biomarker for tobacco smoke consumption/exposure due to its greater sensitivity and specificity, as well as its relatively long half-life (16-20 hours) compared to other biochemical tests (Mourino et al., 2022). The concentration of cotinine in urine is relatively higher, around 4-6 times, compared to blood or saliva, making cotinine testing in urine much more valid and consistently used compared to testing in blood or saliva (Raja et al., 2016).

Jakarta Barat is the area with the highest number of smokers in the Jakarta Special Capital Region, comprising 29.10% of the total. According to statistics, on average, smokers in Jakarta Barat consume around 73 cigarettes per week, which amounts to approximately 10.4 cigarettes per day. The high percentage of smokers will inevitably lead to an increase in the number of passive smokers (Akbar, 2020).

Various studies have shown that elevated levels of cotinine due to cigarette exposure can increase the risk of health problems, including in passive smokers. Several studies have shown that active smoker profiles such as number, duration, and location of consumption, as well as certain types of occupation are known to be associated with cotinine levels in urine samples. However, data on the relationship between the presence of cotinine and the profile of secondhand smoke is still very limited (Munawaroh et al., 2021; Pujiono et al., 2022; Simamora & Ronoatmodjo, 2020). This study aimed to identify cotinine in secondhand smoke and its association with socio-environmental conditions, such as occupation, location, and frequency of exposure.

RESEARCH METHOD

This study employed an analytic survey method with a cross-sectional approach and was conducted in the Rawa Buaya area of West Jakarta. The total sample obtained consisted of 53 passive smokers who had never actively smoked and were over 15 years old.

The procedure begins with explaining the research procedure overview and asking the respondents for their willingness to participate in this study. After obtaining informed consent, data collection is carried out using a survey. The data obtained included sex, occupation, exposure location, and frequency of exposure. The frequency of exposure was categorized into three levels: low (exposed a few times a week), moderate (exposed almost every day), and high (exposed several times a day). The survey completion process was accompanied by the researcher to ensure that the data accurately reflected the respondents actual frequency of exposure.

A cotinine examination was performed using fresh urine samples collected in the morning from respondents who had completed the survey. Cotinine identification in the samples was conducted using the Oncoprobe Cotinine Drug Abuse Rapid Test with a cutoff value of 100 ng/mL. The examination procedure begins with homogenizing the urine sample, followed by adding 3 drops of urine to the sample pad. The results are read after a 5-minute incubation

period. The test is considered positive if only one line appears in the control (C) region, and negative if lines appear in both the test (T) and control (C) regions.

The data obtained were analyzed using IBM SPSS Statistics 25. The normality distribution of the research data was tested using the Shapiro-Wilk test. Sex and cotinine data in passive smokers were analyzed using the Chi-Square test to determine the relationship between the two, while occupation, exposure location, and frequency of exposure data were analyzed using the Kruskal-Wallis test to determine if there were differences between two or more groups. If the Kruskal-Wallis test indicated significant differences, a post hoc Mann-Whitney test was conducted. All research data were evaluated using a significance level of 0.05 (p<0.05) and a 95% Confidence Interval (CI).

This study obtained Ethical Clearance approval from the Health Research Ethics Committee, Lembaga Penelitian dan Pengabdian Masyarakat (LPPM), STIK Kesosi, Jakarta No. 02/I/11/LPPM STIK KESOSI/2022.

RESULTS

The identification of cotinine in this study can be seen in Table 1 which shows that out of a total of 53 samples, 36 individuals (67.90%) were positive for cotinine in urine samples, and 17 individuals (32.10%) were negative. The number of secondhand smoke respondents was dominated by females were 40 individuals (75.50%) compared to males were 13 individuals (24.50%). Based on sex, the distribution of positive cases also occurs higher among females, with 28 individuals (77.80%), compared to males, with 8 individuals (22.20%).

The prevalence based on female sex shows positive results in 28 individuals out of a total of 40 female respondents (70.00%). Meanwhile, among male respondents, a smaller incidence is observed, with 8 individuals out of 13 (61.50%). Statistical analysis indicates non-significant results (p=0.570) regarding the association between sex and cotinine identification in the urine of passive smokers.

Sav	Cotinine Test I	12		
SCA	Positive (+)	Negative (-)	Р	
Female	28	12	0.570	
Male	8	5	0.570	
: Identification of Coti	nine based on Occupation usi	ng Kruskal-Wallis test		
: Identification of Coti	nine based on Occupation usi Cotinine Test R	ng Kruskal-Wallis test Results (N=53)		
: Identification of Coti Occupation	nine based on Occupation usi Cotinine Test R Positive (+)	ng Kruskal-Wallis test Results (N=53) Negative (-)	р	
: Identification of Coti Occupation Housewife	nine based on Occupation usi Cotinine Test R Positive (+) 16	ng Kruskal-Wallis test Results (N=53) Negative (-) 8	р	
: Identification of Coti Occupation Housewife Retailer	nine based on Occupation usi Cotinine Test R Positive (+) 16 11	ng Kruskal-Wallis test Results (N=53) Negative (-) 8 4	p 0.861	

Table 1. Identification of Cotinine based on Sex using Chi-square test

The distribution of respondent's occupations in Table 2 indicates that 24 individuals (45.30%) work as housewives, 15 individuals (28.30%) as retailers, and 14 individuals (26.40%) as students. The prevalence of cotinine examination results based on occupation shows positive results in 16 out of 24 housewives (66.70%), 11 out of 15 retailers (73.30%), and 9 out of 14 students (64.30%). Statistical analysis indicates a significance value of p=0.861, which means there is no meaningful association between occupation and cotinine identification in the urine of passive smokers.

Exposure Location	Cotinine Test Results		р	
	Positive (+)	Negative (-)	Kruskal-Wallis	Mann-Whitney
Home (H)	18	3	< 0.001	PA:<0.001
				B: 0.770
Public Area (PA)	2	12		H:<0.001
				B:<0.001
Both (B)	16	2		H: 0.770
				PA:<0.001

Table 3. Identification of Cotinine by Exposure Location (N=53)

Table 3 also indicates the locations where passive smokers were exposed in this study, namely at home (21 individuals; 39.60%), in public places (14 individuals; 26.40%), and both (18 individuals; 34.00%). Cotinine urine identification based on exposure location shows a high level of positive incidence occurring at home (18 out of 21 individuals; 85.70%), compared to public places (2 out of 14 individuals; 14.30%). Meanwhile, respondents exposed to both locations have the highest positive incidence rate, reaching 88.90% (16 out of 18 individuals). The results of statistical tests indicate a significant influence between exposure location and cotinine identification in urine samples of passive smokers (p<0.001). Further tests show significant results between exposure locations at home and public area (p<0.001), as well as between public area and both (p<0.001).

Exposure Frequency	ency Cotinine Test Results		р		
-	(+)	(-)	Kruskal-Wallis	Mann-Whitney	
Low (L)	3	11	< 0.001	M: 0.009	
				H:<0.001	
Moderate (M)	13	6	_	L: 0.009	
				H: 0.007	
High (H)	20	0	_	L:<0.001	
				M: 0.007	

Table 4. Identification of Cotinine by Frequency of Exposure

An overview of the frequency of exposure in all respondents can be seen in Table 4, which shows a low exposure level in 14 individuals (26.40%), moderate exposure in 19 individuals (35.80%), and high exposure in 20 individuals (37.70%). Cotinine urine identification indicates that the high exposure category has the highest incidence of positive cotinine urine, reaching 100% in all participants in this category (20 individuals). Furthermore, the moderate category shows positive results in 13 out of 19 individuals (68.40%), while the low category has 3 out of 14 individuals (21.40%). Statistical analysis indicates an influence of exposure frequency on cotinine urine identification in samples (< 0.001; p<0.05; Kruskal-Wallis Test). Further statistical tests show a significant influence of all exposure frequency categories on cotinine urine identification (p<0.05; Mann-Whitney Test).

DISCUSSION

This study demonstrates that out of a total of 53 samples, 36 (68.00%) were identified to contain cotinine in their urine samples. This finding indicates high nicotine consumption from secondhand smoke exposure among the participants, leading to increased accumulation of cotinine in urine samples due to its relatively long half-life. This study shows that the number of female respondents is higher than that of males. This finding aligns with several studies indicating that women and children are more likely to be passive smokers, while men are more likely to be active smokers. This is because cigarette consumption behavior is often associated with masculinity, resulting in a higher number of active smokers among men compared to women (Kusumawardani et al., 2020; Munawaroh et al., 2021; Murniasih, 2024). Although the positive cotinine levels in females appear higher than in males, this difference is not statistically significant. This means that male and female passive smokers have the same risk of cotinine

identification in their urine. However, further studies with a proportional comparison of sex numbers are needed for more robust results.

The high number of women who are passive smokers aligns with the higher identification of cotinine among housewives compared to other occupations. This is not only due to the greater number of housewives but also because they are highly vulnerable to exposure to cigarette smoke residue on various household items due to their extensive activities at home (Indrawati & Martini, 2021; Na et al., 2022). Lower cotinine identification occurs among retailers. This is because smoke exposure in this group heavily depends on their customers and colleagues. Additionally, their more active movement and not staying in one place, as well as being relatively in open spaces, reduces their exposure risk compared to housewives. On the other hand, the lowest cotinine identification among students is likely due to their social environment. Generally, students engage in more outdoor activities compared to other groups, so their social environment significantly influences their exposure due to high levels of interaction with friends. Despite these different patterns, these three groups have the same risk of cotinine identification in their urine samples. This result indicates that occupation does not significantly influence the presence of cotinine in urine (Alkhalaf et al., 2021; Indrawati & Martini, 2021).

Exposure location is a significant factor affecting the presence of cotinine in urine. Passive smokers exposed at home show a higher and more significant positive result compared to those exposed in public places. This may occur because cigarette smoke can linger longer in enclosed spaces like homes due to poor air circulation, while smoke exposure in public places is more likely to be in open areas, allowing the smoke to dissipate more quickly. Additionally, passive smokers exposed at home have a higher risk of exposure because cigarette smoke and its derivatives can adhere to various objects within the home (Kusumawardani et al., 2020; Martayani, 2020; Nurjanah et al., 2014; Nurwidayanti & Wahyuni, 2013).

Another factor, such as the frequency of exposure, also significantly affects cotinine identification in urine samples. This condition is demonstrated by the significant cotinine identification results across all groups. The risk increases with the rising frequency of cigarette smoke exposure among passive smokers. Passive smokers with high exposure levels are the most vulnerable to health problems caused by smoking, as indicated by the 100% cotinine identification rate in the urine samples of this group. This condition shows that the urinary cotinine levels in this group exceed 100 ng/mL, which is comparable to the levels found in active smokers. Cotinine identification in the low-exposure category shows a significantly lower risk compared to the moderate and high-exposure categories (Martayani, 2020; Nurjanah et al., 2014; Nurwidayanti & Wahyuni, 2013; Roza & Nopriani, 2024).

This significant result may occur because increased frequency of exposure leads to a higher accumulation of nicotine, which is subsequently converted into cotinine in the body. The high rate of cotinine production due to the increased frequency of exposure cannot be eliminated by the body because of cotinine's relatively long half-life (16-20 hours), resulting in elevated accumulation of cotinine in the urine (Mourino et al., 2022).

Cotinine is the main metabolite of nicotine found in cigarettes, including in smoke and its residue. Research conducted by Nurjanah et al., 2014, indicates that urinary cotinine levels are associated with decreased lung function. High levels of cotinine in the body can cause health problems, such as reduced cognitive and motor function in infants, and decreased psychomotor and concentration abilities in children during their school time (Chen et al., 2013; Lee et al., 2019; Tan et al., 2021). The accumulation of cotinine can affect the balance of several reproductive hormones, such as Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH). Cotinine also impairs lung function and increases the risk of cardiovascular disorders (Canipari et al., 2020; Nurjanah et al., 2014; Omolaoye et al., 2022). Thus, besides being a marker of high exposure to cigarette smoke and its derivatives, the presence of cotinine can also indicate a high health risk for both passive and active smokers.

CONCLUSION

Environmental and social conditions are related to the identification of cotinine in the urine of passive smokers. Factors such as exposure location and frequency demonstrate a strong correlation with the identification of cotinine in the urine samples of passive smokers. Meanwhile, other factors such as sex and occupation show a weaker correlation. Therefore, further efforts are needed to reduce secondhand smoke exposure among passive smokers by enforcing smoke-free area regulations and conducting educational activities to raise awareness of the adverse effects of secondhand smoke. The findings of this study must be further investigated through quantitative research to assess the impact of socio-environmental factors on cotinine levels among passive smokers. Additionally, further research is necessary to explore various other factors that may influence cotinine levels among passive smokers. This is crucial to ensure that the available data is more comprehensive, thus allowing prevention efforts to be more targeted.

ACKNOWLEDGMENTS

The authors would like to thank all those who supported the successful execution and completion of this research.

CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest regarding the publication of this article. All authors have no personal or professional affiliations that could be perceived as having influenced the research. The authors are solely responsible for the content and the conclusions drawn from the research.

REFERENCES

- Akbar, A. (2020). Perilaku Perokok DKI Jakarta 2019. <u>https://satudata.jakarta.go.id/statistik-sektoral/detail?kategori=artikel&page_url=perilaku-perokok-dki-jakarta-2019</u>
- Alkhalaf, M., Suwyadi, A., AlShamakhi, E., Oribi, H., Theyab, Z., Sumayli, I., Yassin, A., Aqeeli, A., Alqassim, A., & Mohamed, H. (2021). Determinants and Prevalence of Tobacco Smoking among Medical Students at Jazan University, Saudi Arabia. *Journal of Smoking Cessation*, 2021, e20. <u>https://doi.org/10.1155/2021/6632379</u>
- Amalia, N. (2021). Efektivitas Penggunaan Media Leaflet Pencegahan Secondhand Vape Smoker Terhadap Risiko Secondhand Vape Smoker di UMKT. Borneo Studies and Research, 2(3), 1900–1907.
- Amelia, S. P., Sopiah, P., & Ridwan, H. (2023). Hubungan Patologi dan Patofisiologi pada Individu Akibat Normalisasi Perilaku Merokok di Indonesia. Jurnal Keperawatan Abdurrab, 7(1), 23–28. <u>https://doi.org/10.36341/jka.v7i1.3360</u>
- Canipari, R., De Santis, L., & Cecconi, S. (2020). Female Fertility and Environmental Pollution. *International Journal of Environmental Research and Public Health*, 17(23), 8802. <u>https://doi.org/10.3390/ijerph17238802</u>
- Chen, R., Clifford, A., Lang, L., & Anstey, K. J. (2013). Is Exposure to Secondhand Smoke Associated with Cognitive Parameters of Children and Adolescents?-a Systematic Literature Review. *Annals of Epidemiology*, 23(10), 652–661. https://doi.org/10.1016/j.annepidem.2013.07.001
- Indrawati, A. L., & Martini, S. (2021). Relationship between Exposure to Cigarette Smoke in Houses and The Incidence of Hypertension in Housewives. *Jurnal Berkala Epidemiologi*, 9(2), 175–183. https://doi.org/10.20473/jbe.v9i22021.175–183
- Kusumawardani, R. D., Suhartono, S., & Budiyono, B. (2020). Keberadaan Perokok dalam Rumah sebagai Faktor Risiko Kejadian Pneumonia pada Anak: Suatu Kajian Sistematik.
- Lathifah, Q. A., Hermawati, A. H., & Putri, A. Y. (2020). Gambaran Nikotin pada Perokok Pasif di Kabupaten Tulungagung: Nicotine in Passive Smokers in Tulungagung Regency. *Borneo Journal of Medical Laboratory Technology*, 3(1), 178–182. <u>https://doi.org/10.33084/bjmlt.v3i1.1594</u>
- Lee, M., Ha, M., Hong, Y.-C., Park, H., Kim, Y., Kim, E.-J., Kim, Y., & Ha, E. (2019). Exposure to Prenatal Secondhand Smoke and Early Neurodevelopment: Mothers and Children's Environmental Health (MOCEH) Study. *Environmental Health*, *18*, 1–11.

- Martayani, A. A. S. D. D. (2020). Hubungan Paparan Asap Rokok dengan Risiko Pneumonia pada Balita di Kabupaten Gianyar. Jurnal Penelitian Dan Kajian Ilmiah Kesehatan Politeknik Medica Farma Husada Mataram, 6(1), 66–74. <u>https://doi.org/10.33651/jpkik.v6i1.55</u>
- Mourino, N., Ruano-Raviña, A., Varela Lema, L., Fernández, E., López, M. J., Santiago-Pérez, M. I., Rey-Brandariz, J., Giraldo-Osorio, A., & Pérez-Ríos, M. (2022). Serum Cotinine Cut-Points for Secondhand Smoke Exposure Assessment in Children Under 5 Years: A Systemic Review. *PloS One*, 17(5), e0267319. https://doi.org/10.1371/journal.pone.0267319
- Munawaroh, M., Nugrahawati, L. R., & Furqaani, A. R. (2021). Scoping Review: Pengaruh Paparan Asap Rokok terhadap Kadar Kotinin dalam Tubuh Perokok Pasif. *Jurnal Integrasi Kesehatan & Sains*, *3*(2), 233–238. https://doi.org/10.29313/jiks.v3i2.7449
- Murniasih, E. (2024). Rokok dan Dampaknya Terhadap Kesehatan. Initium Community Journal, 4(1), 27-33.
- Na, J., Chen, H., An, H., Li, N., Yan, L., Ye, R., & Li, Z. (2022). Association of Rare Earth Elements with Passive Smoking among Housewives in Shanxi Province, China. *International Journal of Environmental Research and Public Health*, 19(1), 559. <u>https://doi.org/10.3390/ijerph19010559</u>
- Nurjanah, Kresnowati, L., & Mufid, A. (2014). Gangguan Fungsi Paru dan Kadar Cotinine pada Urin Karyawan yang Terpapar Asap Rokok Orang Lain. *Jurnal Kesehatan Masyarakat*, 10(1), 43–52.
- Nurwidayanti, L., & Wahyuni, C. U. (2013). Analisis Pengaruh Paparan Asap Rokok di Rumah pada Wanita terhadap Kejadian Hipertensi. *Jurnal Berkala Epidemiologi*, 1(2), 244–253.
- Oktaviyanti, R. P., Sari, A. I. P., Puteri, R., & Utami, N. K. (2023). Hubungan Kebiasaan Merokok Bagi Kesehatan dan Daya Tahan Tubuh. *JIKES: Jurnal Ilmu Kesehatan*, 1(2), 196–202.
- Omolaoye, T. S., El Shahawy, O., Skosana, B. T., Boillat, T., Loney, T., & Du Plessis, S. S. (2022). The Mutagenic Effect of Tobacco Smoke on Male Fertility. *Environmental Science and Pollution Research*, 29(41), 62055– 62066. <u>https://doi.org/10.1007/s11356-021-16331-x</u>
- Pujiono, F. E., Solikah, P., & Mulyati, T. A. (2022). Cotinine Analysis in Active Smoker's Urine by Immunochromatography Assay Method. Jurnal Sintesis: Penelitian Sains, Terapan Dan Analisisnya, 3(1), 43– 48. <u>https://doi.org/10.56399/jst.v3i1.52</u>
- Raja, M., Garg, A., Yadav, P., Jha, K., & Handa, S. (2016). Diagnostic Methods for Detection of Cotinine Level in Tobacco Users: a Review. *Journal of Clinical and Diagnostic Research: JCDR*, 10(3), ZE04. <u>https://doi.org/10.1371/journal.pone.0267319</u>
- RISKESDAS. (2019). Riset Kesehatan Dasar 2018.
- Roza, S., & Nopriani, Y. (2024). Hubungan Paparan Asap Rokok dengan Kejadian Hipertensi pada Lansia. *Jurnal Kesehatan Tambusai*, 5(1), 2223–2225.
- Said, M., & Muluki, M. (2022). Karakteristik Pengguna Rokok Elektrik (Vapor) Di Wilayah Parepare. Jurnal Ilmiah Manusia Dan Kesehatan, 5(1), 459–467. <u>https://doi.org/10.31850/makes.v5i1.635</u>
- Sandhi, S. I. (2019). Studi Fenomenologi: Kesadaran Diri (Self Awareness) Perokok Aktif yang mempunyai Anak Balita dalam Perilaku Merokok di Tempat Umum di Kelurahan Pegulon Kabupaten Kendal. *Jurnal Kebidanan Harapan Ibu Pekalongan*, 6, 237–243. <u>https://doi.org/doi.org/10.37402/jurbidhip.vol6.iss2.61</u>
- Simamora, S. E. D., & Ronoatmodjo, S. (2020). Hubungan Paparan Asap Rokok dari Suami pada Wanita Usia 15-57 Tahun dengan Kejadian Bayi Berat Lahir Rendah di Indonesia (Analisis Data Lanjutan IFLS-5 tahun 2014). *Jurnal Kesehatan Reproduksi*, *11*(1), 89–100. <u>https://doi.org/10.22435/kespro.v11i1.2753.89-100</u>
- Subagya, A. R. (2023). Perokok Aktif dan Perokok Pasif. Bumi Aksara.

- Tan, X., Vrana, K., & Ding, Z.-M. (2021). Cotinine: Pharmacologically Active Metabolite of Nicotine and Neural Mechanisms for its Actions. *Frontiers in Behavioral Neuroscience*, 15, 758252. <u>https://doi.org/10.3389/fnbeh.2021.758252</u>
- Tanuwihardja, R. K., & Susanto, A. D. (2012). Rokok Elektronik (Electronic Cigarette). Jurnal Respirasi Indonesia, 32(1), 53–61.
- Tarigan, I. U., & Yulianti, A. (2019). Gambaran Kesadaran Masyarakat terhadap Kawasan Tanpa Rokok di Indonesia. Jurnal Penelitian Dan Pengembangan Pelayanan Kesehatan, 123–130. https://doi.org/doi.org/10.22435/jpppk.v3i2.2655
- Tzatzarakis, M. N., Vardavas, C. I., Terzi, I., Kavalakis, M., Kokkinakis, M., Liesivuori, J., & Tsatsakis, A. M. (2011). Hair Nicotine/Cotinine Concentrations as a Method of Monitoring Exposure to Tobacco Smoke among Infants and Adults. *Human & Experimental Toxicology*, 31(3), 258–265. https://doi.org/10.1177/0960327111422401