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Effect of passive tobacco smoke on the incidence of respiratory adverse events in female patients undergoing general anesthesia– a cohort study

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Abstract

Background Passive smoking is linked to increased respiratory adverse events (AEs) during general anesthesia (GA). This study aims to assess whether females exposed to passive tobacco smoke undergoing GA, experience a higher incidence of perioperative respiratory AEs.

Methods This single-center prospective cohort study was conducted from July 2021 to July 2022, at a University Hospital. After approval from the ethical review committee, 150 female patients receiving GA for elective surgeries requiring endotracheal intubation were included and classified into Passive Smoking Exposure (PSE) and Non-Passive Smoking Exposure (NPSE) groups. Data on respiratory adverse events (AEs) including laryngospasm, bronchospasm, breath holding, desaturation, hypersecretion, coughing, wheezing, and stridor during the perioperative period was collected using a proforma. Statistical analysis was performed using RStudio with Chi-square, Fisher's exact test, and Mann-Whitney U test to determine significance.

Results Among 150 female participants, 75 were included in the PSE and 75 in the NPSE groups. The PSE group had an overall statistically significant incidence of respiratory AEs compared to the NPSE group (69.3 vs. 16.0%, $p < 0.001$). Hypersecretion (50.7% vs. 4%) and desaturation (38.7% vs. 6.7%) intraoperatively and desaturation (14.7% vs. 1.3%) and cough (10.7% vs. 0%) in the post-anesthesia care unit (PACU) were significantly more common in the PSE group ($p < 0.001$). At 12 h postoperatively, 56% of the PSE group had respiratory issues versus 32% in the NPSE group ($p < 0.05$).

Conclusion Passive smokers had a significantly higher incidence of perioperative respiratory AEs with GA, necessitating the need for preoperative strategies to address passive smoke exposure.

Keywords Passive smoking, Laryngospasm, Women, General anesthesia

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Background

Cigarette smoking is an environmental and social concern and a threat to health whether done actively or passively [1]. Passive smoking, also known as second-hand smoke exposure, is an involuntary smoking which occurs when non-smokers inhale tobacco smoke from their environment. Passive tobacco smoke exposure and its implications are a worldwide challenge and a health hazard being recognized in recent times [1]. A Passive smoker is exposed to inhalation of cigarette smoke by being in the vicinity of a primary smoker and is exposed not only to the smoke from the primary smoker but also to a side stream emitted directly from the burning end of a cigarette, cigar, or pipe (often more toxic, as it is unfiltered) and constitutes about fourth-fifth (80%) of the smoke [1].

Key Characteristics of passive smoking: (1) Involuntary exposure, as individual does not actively smoke but is affected by others' tobacco use, (2) Environments where it occurs are homes, vehicles, public spaces, or workplaces where smoking occurs. 3)Health risks are directly linked to respiratory infections, lung cancer, cardiovascular disease, and exacerbated asthma. Studies have shown that active smokers and those exposed to passive tobacco smoke can develop respiratory adverse events (AE) when exposed to general anesthesia (GA) due to chronic changes in their airways due to tobacco smoke exposure [2]. Exposure to cigarette smoke is linked to greater postoperative morbidity because of greater anesthetic requirements and respiratory complications [3–5]. Studies done on the effects of passive smoking in adults undergoing GA have shown conflicting results [2, 4].

Women belong to a vulnerable group of the population, that is exposed to passive tobacco smoke, especially in developing countries and there is limited research in this group [2]. A study has observed that females are more sensitive and vulnerable to tobacco smoke than males, indicating that they could have a higher rate of respiratory AE when undergoing GA [2, 6].

According to a WHO report, in developing countries majority of the smokers are males due to cultural and social reasons. In these regions especially Asia and the Pacific region, females and children become the victims of passive tobacco smoke exposure at homes and outside their homes [7]. According to the statistics, in Pakistan 27.0% of smokers are males and 5.5% are females in a 5:1 ratio thus indicating the high burden of passive tobacco smoke exposure in this group which may lead to preventable health issues including perioperative adverse events [8].

Therefore, the rationale of our study is to see if this high risk group of females who are subjected to passive tobacco smoke exposure have an increased frequency of respiratory AE while undergoing GA so that suggestions regarding preoperative cessation of passive smoke exposure can be made in case of a positive association between passive tobacco exposure and perioperative respiratory AEs since it is not routinely practiced.

The primary objective of our study is to compare the frequency of respiratory AEs in females exposed to passive tobacco smoke exposure to those females who are not exposed to passive tobacco smoke exposure undergoing GA.

Materials and methods

Study design

This single-center prospective cohort study was conducted from 30 July 2021 to 30 July 2022 after approval by the Ethics Research Committee of The Aga Khan University Hospital (Approval no 2020-3672-14238).

Study population

The study sample included 150 participants, and the study population was female patients undergoing elective surgery at the Aga Khan University Hospital. The inclusion criteria included non-smoker female patients (both passive or nonpassive smokers), who were born as females (sex), between the ages of 18 and 65 years, belonging to the American Society of Anesthesiologists (ASA) I and II category, with a body mass index (BMI) of <35 kg/m^2 undergoing elective surgery under GA requiring endotracheal intubation. Included patients were grouped according to their history of either being exposed or not exposed to passive smoking (1) Passive smoking exposure (PSE) group or (2) Non passive smoking exposure (NPSE) group. The exclusion criteria included patients undergoing cardiac /thoracic surgery, or any surgery in proximity of airways that can precipitate respiratory events due to airway stimulation, having active, chronic or a 4-week history of any respiratory or airway disease, history of difficult airway, tracheostomy, active smokers, and patients who had left smoking within the past 5 years.

Data collection, exposure, and outcome

Participants were selected using a non-probability consecutive sampling technique and were assessed a day prior to the surgery for eligibility in the study by one of the investigators. Those patients fulfilling the inclusion criteria were explained the purpose of the study and were asked for written informed consent was obtained from all participants. All participants were advised that they could withdraw, or not participate, without any effect on their clinical care. The questionnaires never sought sensitive personal information, and no biological samples were taken. The consenting participants were allocated into groups depending on their status of exposure to passive smoke into NPSE or PSE groups.

Nonpassive smokers belonging to the NPSE group were defined as patients who did not have exposure to passive smoking, or it was less than 1 cigarette per day or less than 3 consecutive months.

Participants having had exposure to passive tobacco smoke in the previous 24 h and having had exposure to passive smoking for at least 3 consecutive months were included in the PSE group. These participants were evaluated for their extent of exposure to passive smoking by questions pertaining to participants living or working with a smoker and exposure to involuntary inhalation of smoke in the same household or within 10 feet of a working place and if they were not able to change their environment. The degree of exposure was determined by the number of cigarettes passively smoked according to the patient's history. The degree of exposure was thus self-reported.

Data collection was done in the form of a questionnaire which was denoted by serial number that was unique to every participant and distributed and collected in enclosed envelopes by principal investigators. Blinding was ensured and the physicians and nurses involved in intraoperative and postoperative assessment were not aware of the patient's passive smoke exposure status. All participants included in the study were anesthetized in a standard manner by an experienced anesthesiologist who was accompanied by an anesthesia resident. Routine monitoring including electrocardiogram, noninvasive arterial blood pressure, peripheral oxygen saturation (SpO_2) using a pulse oximeter temperature monitoring using a temperature probe, and end-tidal CO_2 ($EtCO_2$) monitoring using capnography was done in the operating room. A twenty-gauge intravenous cannula was inserted, and induction of anesthesia was done via intravenous induction with Propofol 2.0 mg/kg body weight followed by maintenance with Isoflurane 1–1.5% in Oxygen-Nitrous oxide (40-60%) or Oxygen-Air (40- 60%). Airway control was performed by mask and Guedel airway was used if needed. Controlled mechanical ventilation was achieved with endotracheal intubation. All intubated patients received a nondepolarizing neuromuscular blocking agent Cisatracurium (0.15 mg/kg) before intubation after bag-mask ventilation of 3 min and 30 s or a depolarizing muscle relaxant, Succinylcholine (0.15 mg/kg) for rapid sequence induction which was followed by a non-depolarizing muscle relaxant (Cisatracurium) for the rest of the surgery. Before extubation, the neuromuscular block was reversed with neostigmine (2.5 mg) and glycopyrrolate (0.5 mg). Anesthesia duration (time from the induction to extubation), surgical duration (time from incision and dressing), mode of perioperative analgesia (parenteral and /or epidural and /or nerve blocks), and mode of induction (rapid sequence or bag mask induction) was recorded for both groups.

Occurrence of respiratory AEs were recorded as primary outcome measures three times (1) Intraoperative period during induction and emergence from anesthesia (2) Post-anesthesia recovery period in the post-anesthesia care unit (PACU) and (3) At 12 h post-surgical period.

1) Respiratory AEs for the intraoperative period were recorded in the operating room (OR) and for the immediate post-anesthetic period in the PACU. The respiratory AEs included any incidence of (1) laryngospasm (assessed and measured as the inability to breathe, failure to ventilate the patient, and /or need of continuous positive pressure to maintain ventilation and/or requirement of additional doses of muscle relaxants) (2) bronchospasm (assessed and measured as: difficulty in breathing or ventilation and /or wheeze on auscultation and/or increase in peak airway pressure) (3) breath holding (more than 15 s), (4) desaturation (assessed and measured as: oxygen saturation below 95%), (5) hyper secretion (assessed and measured as: the increase of quantity and density of secretions requiring endobronchial suctioning /oral or nasal suctioning more than two times) (6) cough (assessed and measured as: more than 3 episodes or one episode lasting more than15 seconds) (7) Wheeze or stridor (assessed and measured clinically. Wheeze: The presence of a whistling sound at the expiration phase of breathing mainly due to lower airway obstruction. Stridor: Sound produced due to upper airway obstruction leading to decreased flow of air through the narrowed passage.) All these events were accepted as respiratory AEs during the intraoperative and postoperative periods.

Each respiratory AE was recorded separately but regardless of the number of respiratory AEs in each participant, it was taken as 1 event of respiratory AE. The occurrence of respiratory AE was assessed intraoperatively by the anesthesiologist who anesthetized the patient and in the PACU by the PACU nurse or the anesthesiologist appointed in the PACU according to the defined criteria for each variable. Both assessors were blinded to the passive smoking group. All the AEs were treated according to hospital/departmental protocols.

After surgery, patients were shifted from OR to PACU where Modified Aldrete Score (MAS) was used to evaluate the patients on arrival and discharge. Patients were discharged from PACU to post-surgical ward when MAS was equal to or more than nine which is the accepted score for a patient's discharge from PACU. Additional data collected included MAS on admission to PACU and upon discharge from PACU and duration of stay at PACU.

After the surgery, the patient was followed in the ward for admitted patients or through telephonic communication for 12 h to assess the development of any major respiratory complication e.g. sore throat, upper respiratory tract infection, wheezing, stridor, and cough. These respiratory complications were observed and documented by the attending nurse in the patient chart for admitted patients and for daycare patients who were discharged these complications were self-reported by the patient on a telephonic call. This was documented and analyzed separately as an addition to the perioperative complications.

Statistical analysis

The sample size was determined referencing a prior investigation by Esen Simsek et al., which found that the incidence of respiratory complications during GA was 25.1% in the exposed group and 8.4% in the unexposed group [2]. With a significance level of 5% and a test power of 99% (one-sided), the sample size was calculated to be 150 (75 participants in each group).

The data analysis was conducted using RStudio (version 4.1.2; Boston, USA). The Shapiro-Wilk or Kolmogorov-Smirnov test was employed to assess the normality assumption for numerical variables such as age, weight, height, and duration of passive smoke exposure. Results indicated asymmetry in all variables, leading to the computation of the median (interquartile range) for these variables. Qualitative variables like procedure, type of surgery, ASA status, and frequency of passive smoke exposure were analyzed by computing frequency and percentage. Stratification analysis was then carried out based on passive smoker exposure (PSE) and non-passive exposure (NPSE) groups. For assessing the significance of differences, Chi-square or Fisher's exact test was applied to qualitative variables, while the Mann-Whitney U test was utilized for numerical variables. A p-value of ≤ 0.05 was considered indicative of statistical significance.

Results

A total of 152 participants were eligible to participate in the study and 2 refused to participate due to unwillingness to be a part of a research project. One Hundred and fifty participants were included after taking an informed consent. They were classified into two groups with 75 participants in the PSE and 75 participants in the NPSE group. Figure 1 is the consort diagram depicting the recruitment of participants, their classification, and analysis. No statistically significant difference was found between the demographic variables of the PSE and NPSE groups (Table 1).

Comparative analysis of effect modifiers variables including anesthesia duration, surgical duration, mode of analgesia, mode of induction, and MAS on admission to PACU and upon discharge from PACU and duration of stay at PACU was done. There was no statistically significant difference among these variables with the p value > 0.05 (Table 2).

The incidence of overall respiratory AEs used as a measure of comparison of frequency of respiratory AEs was 69.3% (52 out of 75 participants) in the PSE group n 16.0% (12 out of 75 participants) in the NPSE group. This finding was statistically significant (p-value < 0.001).

While comparing different respiratory AEs in the intraoperative period, a statistically significant difference (p-value < 0.001) was observed for hypersecretion between the two groups (50.7% in the PSE vs. 4% in the NPSE) and incidence desaturation (38.7% in the PSE vs. 6.7% in the NPSE). The comparison between spasm, cough, and breath holding showed no statistically significant difference between the groups (Table 3).

Recorded respiratory AEs in the postoperative period in PACU are shown in Table 3. A statistically significant difference was found in the incidence of desaturation (p-value = 0.005) and incidence of cough (p-value = 0.006). However other variables did not show a statistically significant difference (Table 3).

On following patients 12 h postoperatively 56% patients in the PSE group had respiratory AEs vs. 32% in the NPSE group (p-value < 0.05) The respiratory AEs reported were secretions or rhinitis in 13 (17.3%) patients in PSE group compared to 6 (8.0%) patients in NPSE groups, sore, itchy throat in 15 (20.0%) patients in PSE group compared to 12 (16.0%) patients in NPSE groups, pain in throat in 7(9.3%) patients in PSE group compared 3(4.0%) patients in NPSE groups, cough in 5(6.7%) patients in PSE group compared to 3(4.0%) patients in NPSE groups and desaturation in 2(2.7%)patients in PSE group and none in NPSE group.

A subgroup analysis was done in the PSE group among patients who were exposed to more than 10 cigarettes per day vs. those exposed to an average of equal to or less than 10 cigarettes per day. The p-value was > 0.05 for all variables and thus no statistical difference was found in participants exposed to > 10 or ≤ 10 cigarettes/day.

Discussion

The study was conducted with the aim to find out the association between passive tobacco smoke exposure and respiratory AEs during GA in females since they are greatly exposed to passive tobacco smoke in the developing countries, carrying the risk of high burden of disease. The results of this study showed that females who were passive smokers had a higher incidence of overall respiratory complications as compared to females who were not passive smokers.

The results of this study are comparable to a study by Simsek E et al. which included a cohort of both males and

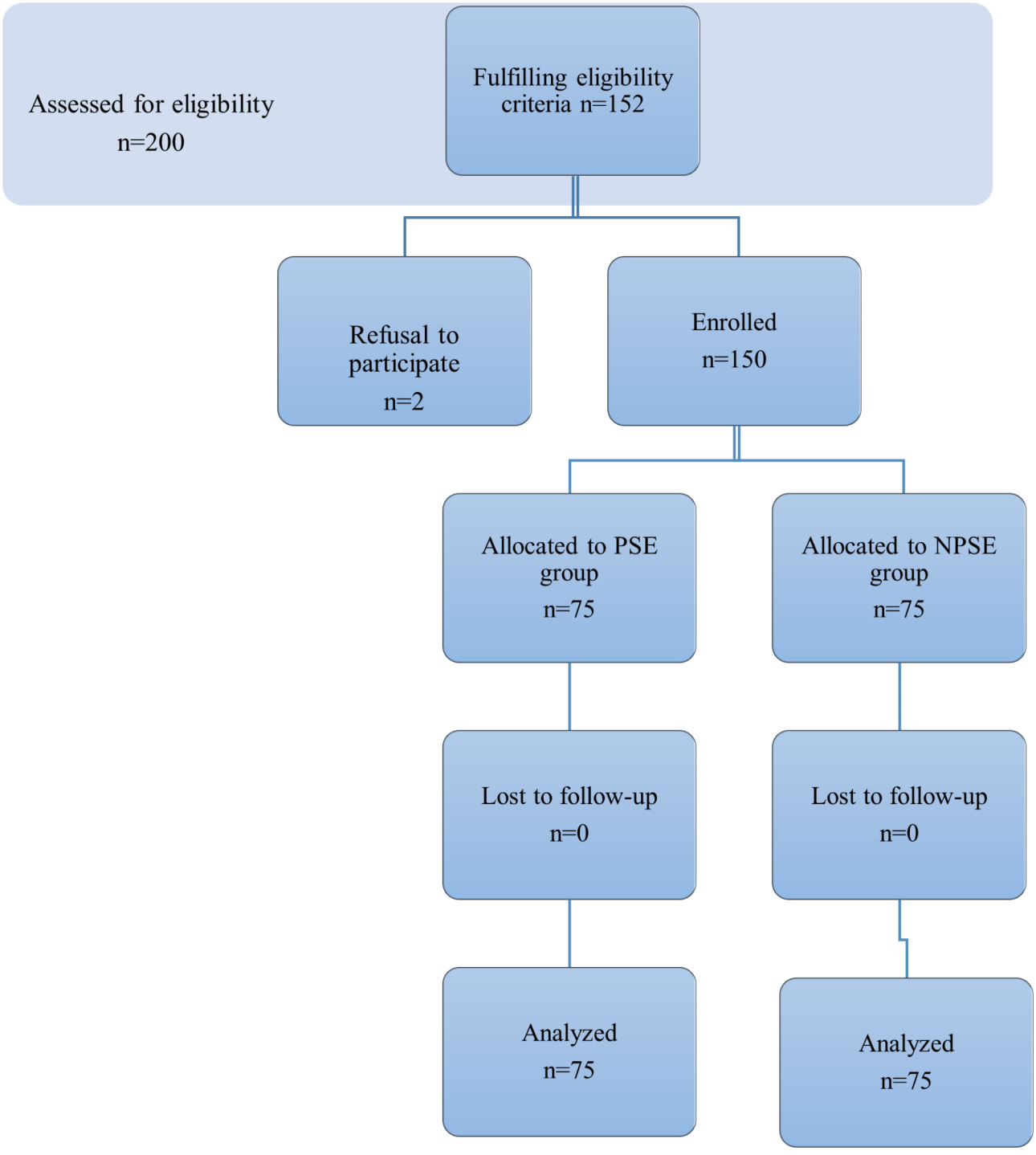

Fig. 1 Consort Diagram depicting recruitment of participants, their classification and analysis

females. The study summarized that a total of 35.2% of patients exposed to passive tobacco smoke had respiratory AEs as compared to 8.4% in the non-exposed (control) group, p-value = 0.001. These findings are similar to our study where 69.3% of exposed and 16% of patients in the unexposed groups had overall respiratory AEs [2]. The study by Simsek et al. also showed that out of those who developed respiratory complications, 82.5% were females and 17.5% were males. This was statistically insignificant but indicated that women were more sensitive to the effects of passive tobacco smoke exposure [2].

A meta-analysis demonstrated a significant association of environmental smoke with increased risk of perianesthetic respiratory AEs (Pooled risk ratio 2.52 CI 95%

Table 1 Comparative analysis of demographics between passive smoker exposure (PSE) & non-passive exposure (NPSE) groups

Variable	PSE (*N* = 75)	NPSE (*N* = 75)	*P*-value
Age (18-65years)[a]			
Median (IQR)	42.0 (32.5, 49.5)	46.0 (34.0, 59.0)	0.144
Weight (kg)[a]			
Median (IQR)	70.0 (59.5, 78.5)	70.0 (59.5, 78.5)	0.161
Height (cm)[a]			
Median (IQR)	157 (154, 160)	156 (150, 160)	0.552
BMI (< 35 kg/m^2)[a]			
Median (IQR)	28.7 (24.4, 31.2)	27.3 (23.9, 30.1)	0.230
ASA (I-II)[b]			0.980
I	15 (20.0%)	14 (18.7%)	
II	60 (80.0%)	61 (81.3%)	

Note: A; Mann-Whitney U test, B: Chi-square or Fisher's exact test

PSE: passive smoke exposure, NPSE: Non-passive smoke exposure

1.68 to 3.77) among children aged 0–18 years [9]. In this meta-analysis, 15 out of 28 research articles were on anesthesia outcomes like the ones used in our study on female patients with significant association of respiratory AEs among passive smokers.

In one study, the effect of passive smoking on carboxy hemoglobin (CO Hb), arterial oxygen pressure (PaO2), arterial carbon dioxide pressure (PaCO2) levels, and perioperative adverse respiratory AEs under GA was compared among children having smoker versus non-smoker parents [10]. COHb levels in children who were passive smokers were found to be higher compared to the group who did not smoke. Although no difference was found in terms of complications that occurred during anesthesia, the frequency of asthma was found to be higher, especially in the group in which both parents were smokers, and PCO2 values were found to be higher in the groups who smoked compared to the group who never smoked. This suggested that parental smoking affected the lung functions of the children negatively [10].

In our study, we also compared the frequency of passive tobacco smokers. In the exposed group, subgroup analysis was done. One group had an exposure of > 10 cigarettes/day and the other group had an exposure of < 10 cigarettes/day. In this study, no significant difference was found in both groups for any of the respiratory AEs. This finding contrasted with the findings in the study by Simsek E et al. where exposure to > 10 cigarettes/day led to greater perioperative respiratory AEs (p-value < 0.05) [9]. This finding is also in contrast to a study conducted by Skolnick et al. in which it was found that with increasing levels of urinary cotinine in children exposed to tobacco smoke, the incidence of respiratory adverse events during the perioperative period increased. The contrast is likely due to the self-reported history and variation in day-to-day exposure and thus the history being an estimate of average daily exposure leading to variation in the results [9].

The limitations of our study were that the degree of tobacco smoke exposure was self-reported by the patient and thus dependent on memory recall rather than objective means to measure the degree of exposure to Tobacco smoking. This recall bias could have led to underestimation of the tobacco smoke exposure. Another limitation is that the study sample was extrapolated from a single

Table 2 Comparative analysis of effect modifiers variables between passive smoker exposure (PSE) & non-passive exposure (NPSE) groups

Variable	PSE (*N* = 75)	NPSE (*N* = 75)	*P*-value
Anesthesia duration (hours)[a]			
Median (IQR)	2.50 (2.14, 3.78)	2.50 (2.05, 3.44)	0.886
Surgical duration (hours)[a]			
Median (IQR)	2.03 (1.33, 3.13)	2.05 (1.33, 2.56)	0.734
Analgesia[b]			1.000
Parenteral	71 (94.7%)	72 (96.0%)	
Parenteral + Epidural	2 (2.7%)	2 (2.7%)	
Parenteral + Nerve block	2 (2.7%)	1 (1.3%)	
Mode Induction[b]			1.000
Rapid sequence intubation	1 (1.3%)	1 (1.3%)	
Bag mask ventilation	74 (98.7%)	74 (98.7%)	
MAS arrival (score)[a]			
Median (IQR)	11.0 (10.0, 11.0)	11.0 (10.0, 12.0)	0.853
MAS discharge (score)[a]			
Median (IQR)	12.0 (11.0, 12.0)	12.0 (12.0, 12.0)	0.267
Duration of stay PACU (hours)[a]			
Median (IQR)	1.00 (1.00, 1.30)	1.00 (1.00, 1.30)	0.726

Note: A; Mann-Whitney U test, B: Chi-square or Fisher's exact test

PSE: passive smoke exposure, NPSE: Non-passive smoke exposure

Table 3 Comparison of respiratory adverse events during the intraoperative and postoperative phase in PACU between passive smoker exposure (PSE) & Non passive exposure (NPSE) groups

Variable	Exposure (*N* = 75)	Non-Exposure (*N* = 75)	*P*-value
Intraoperative Respiratory AEs			
SPASM[b]	5 (6.7%)	1 (1.3%)	0.209
Secretions[b]	38 (50.7%)	3 (4.0%)	< 0.001
Cough[b]	10 (13.3%)	5 (6.7%)	0.276
Breath holding[b]	2 (2.7%)	2 (2.7%)	0.987
Wheeze or stridor[b]	2 (2.7%)	3 (4.0%)	0.978
Desaturation[b]	29 (38.7%)	5 (6.7%)	< 0.001
Postoperative Respiratory AEs			
SPASM	0 (0%)	0 (0%)	-
Secretions[b]	3 (4.0%)	0 (0%)	0.245
Cough[b]	8 (10.7%)	0 (0%)	0.006
Breath holding	0 (0%)	0 (0%)	-
Wheeze or stridor	0 (0%)	0 (0%)	-
Desaturation[b]	11 (14.7%)	1 (1.3%)	0.005

Note: B: Chi-square or Fisher's exact test

hospital with a relatively smaller sample size. The study was conducted in the immediate years following COVID 19 pandemic and even though any patient with a history of respiratory tract infection having chronic, active, or a 4-week history of any respiratory or airway disease, was excluded but specific history of COVID 19 infection was not sought.

The strength of the study was that multiple variables for respiratory AEs were considered to observe different types of respiratory AEs. Another strength is that subgroup analysis with average cigarette exposure per day and its relation to the development of respiratory AEs was done. No data was found for any previous study conducted on the female population even though they are a vulnerable group exposed to passive tobacco smoke thus adding to the strength of the study.

Conclusion

This study found that females exposed to passive smoking had a significantly higher incidence of respiratory AEs during and after GA compared to those not exposed. Specifically, the PSE group experienced more frequent hypersecretion, desaturation, and cough, both intraoperatively and in the PACU, with a higher rate of complications 12 h postoperatively. The findings suggest that passive tobacco smoke exposure is a notable risk factor for respiratory issues in the perioperative period. However, no significant difference was observed based on the level of passive tobacco smoke exposure. These results highlight the need for heightened awareness and potential preoperative interventions for patients with passive tobacco smoke exposure to mitigate respiratory complications. These interventions include changing location or cessation of smoking by the primary smokers around the patient. Further research is warranted to explore the mechanisms and impacts of varying levels of passive smoke exposure on perioperative respiratory outcomes.

Abbreviations

Respiratory AE	Respiratory adverse event
GA	General anesthesia
PSE	Passive smoke exposure
NPSE	Non-Passive smoke exposure
ASA	American Society of Anesthesiologists
BMI	Body mass index
SpO2	Oxygen saturation
etCO2	End tidal Carbon dioxide
PACU	Post anesthesia care unit
MAS	Modified Aldrete score
OR	Operating room

Supplementary Information

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Supplementary Material 1

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Author contributions

MH contributed to the conceptualization of the study, acquisition of data, and drafting the manuscript. SA was responsible for the conceptualization of study, drafting and revision of the manuscript, and providing overall supervision. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was obtained from the Ethics Research Committee of The Aga Khan University and Hospital (Approval no 2020-3672-14238). A written informed consent was taken from all the enrolled participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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