

## Risk assessment of Gastrointestinal cancer in hookah and opium users

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### Abstract

**Introduction:** Gastrointestinal (GI) cancers prevail in Iran. The existing literature shows the relationship between tobacco and opium consumption and the incidence of this type of cancer. Yet, there is scarce research on the effect of simultaneous consumption of these Substances on cancers, especially GI cancers. Therefore, the present study aimed to test the relationship between hookah and opium smoking and the effects of their simultaneous use on GI cancers in Minab city in Hormozgan province.

**Materials and methods:** The present case-control study was conducted on 60 cases (patients with GI cancers) and 120 controls (healthy residents) of Minab, a city in Hormozgan province. In this study, chi-square and Fisher's exact tests were used to test the difference between the participants' characteristics in the case and control groups. Moreover, the logistic regression model was used to test the relationship between hookah and opium consumption and GI cancers as the main outcome.

**Findings:** The mean  $\pm$  standard deviation of participants' age was  $55.58 \pm 12.80$  (R = 30-81) in the control group and  $56.22 \pm 13.88$  (R = 30-90) in the case group. The prevalence of opium, cigarette, and hookah consumption in the case group was 55%, 40%, and 65%, respectively. In the control group, it was 4.2%, 10%, and 9.2%, respectively. This difference was statistically significant ( $p < 0.001$ ). The results showed that tobacco and opium significantly increase the risk of GI cancers. This risk is increased significantly respectively in participants smoking only cigarettes (OR=5.08), only hookah (OR=17.71), only opium (OR=31.05), opium and hookah simultaneously (OR=65.81), opium and cigarettes simultaneously (OR=77.08) and cigarettes, hookah and opium simultaneously (OR=110.74) ( $p < 0.05$ ).

**Conclusion:** This study showed a significant and positive relationship between opium and tobacco consumption and GI cancers. Considering that cancer prevention is the most affordable strategy in controlling this disease, the present findings help prevent the disease through identifying some risk factors of GI cancers. It is recommended to conduct more detailed studies considering the pattern of smoking and other risk factors.

**Keywords:** Gastrointestinal tract cancer, Hookah, Opium, Hormozgan

## Introduction:

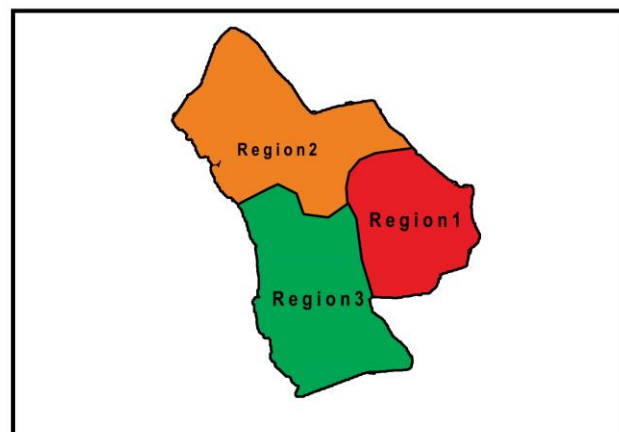
Gastrointestinal (GI) cancers are of great importance in the world due to their high prevalence and mortality rate. These cancers (including malignancies of the esophagus, stomach, small intestine, colon, rectum, pancreas, gallbladder, bile ducts, and liver) account for 1.4 million new cases and 3 million mortalities worldwide on an annual basis (1- 3). As reported by WHO, in 2020, stomach cancer and colorectal cancer were the second and third most prevalent cancers in men and women, with 14,656 and 11,942 cases in Iran (4). Considering the high incidence of these cancers, it is necessary to identify the risk factors of these cancers. In previous studies, non-preventable risk factors have been exemplified as demographic variables, family history and genetic predisposition and preventable risk factors related to lifestyle such as diet, consumption of hot tea, salty foods, presence of nitrates and other trace elements in water or food, cigarette smoking, alcohol consumption, body mass index and Helicobacter infection (5-9). In recent years, experts of the International Agency for Research on Cancer (IARC) declared opium use to be as carcinogenic to humans, as cigarette smoking and alcohol consumption (10). Nevertheless, today in Iran, tobacco and

opium consumption is very common and a major threat to public health. Because of its easy access and belief in its preventive role in diseases, opium is used traditionally, especially in adults and the elderly. Actually, its prevalence reaches 24.7% in some parts of Iran (11-13). Due to the existing misconceptions, in the past few years, tobacco use, especially hookah smoking, has been associated with an increasing rate of consumption, especially in the south of Iran (14). Contrary to the public belief, these Substances have led to a great financial and human burden in many parts of the world (15). There is scientific evidence to show that opium and tobacco use is associated with a number of cancers (16), including GI cancers (17). However, the existing research findings are limited. More evidence is required to establish a causal relationship between opium and tobacco use and the risk of GI cancers. There is a dearth of research on the effect of simultaneous use of tobacco and opium with cancers, especially cancers in the GI tract. Therefore, the present case-control study explored the relationship between hookah and opium smoking and the effects of simultaneous consumption of both on GI cancers in Hormozgan province. The research hypotheses include: 1- Hookah consumption is related to GI cancers. 2- Opium consumption is related to GI cancers. 3- Cigarette smoking is related to GI cancers. 4- The simultaneous use of cigarettes, hookah and opium is related to GI cancers.

## **Materials and Methods:**

### **Research population and Study area**

The present case-control study was conducted on 180 participants. There were 60 participants in the case group suffering from GI cancers (esophagus, stomach, small intestine, large intestine, rectum, pancreas, gall bladder, bile ducts and liver). They were selected from the cancer registration center of Minab health center (incidences in 2018). The selection method was a census. In the control group, there were 120 participants selected among healthy people (in terms of having cancer) residing in Minab. For each case, 2 controls were selected from the nearest neighbors.



**IRAN - Hormozgan - Minab**



fig.1 geographic locations of study areas

Fig 1. Map of studied areas

### **Inclusion and exclusion criteria:**

The inclusion criterion was affliction with GI cancers according to the results of pathology tests. The exclusion criteria were affliction with other cancers or malignancies in other organs, and non-cooperation of the participant. Since the patients with cancer may have used opium to reduce their pain after the onset of the disease, the history of using opium and its derivatives was also an exclusion criterion in those who began using opium less than a year before the diagnosis (18).

**Data collection:** The data were collected using a structured questionnaire including demographic information, information related to the type of cancer and family history of the disease, information related to the history of opium and hookah use in the past ten years. To reduce potential interviewer bias and interpersonal variability, the interview was conducted by a trained interviewer in a friendly environment.

**Ethical Considerations:** The research protocol was approved by the ethics committee of Hormozgan University of Medical Sciences (#IR.HUMS.REC.1397.171), and an informed consent was obtained from all participants.

**Research variables:** In this study, the dependent variable was GI tract cancers (esophagus, stomach, small intestine, colon, rectum, pancreas, gall bladder, bile ducts, and liver) and the independent variables were smoking, hookah use, and opium use. Potential confounders were age, sex, education, occupation and family history of cancer.

**Statistical Analysis:** For data analysis, the chi-square and Fisher's exact tests were used to test the difference between the characteristics of participants in the two groups of case and control. Moreover, regression models were used to test the relationship between tobacco and opium use with gastrointestinal cancers as the main outcome. Adjustment was made for relevant confounders to estimate odds ratios (ORs) and 95% confidence intervals (CIs). All tests were two-tailed and p-values <0.05 were considered statistically significant.

**Results:** In this study, 120 healthy participants acted as the controls and 60 patients were the cases. The latter suffered from GI cancers including stomach cancer 37 (61.67%), small intestine 14 (23.33%), colon 2 (3.33%), liver 6 (10.0%) and esophagus 1 (1.67%). The average age of the control group was  $55.58 \pm 12.80$  (R=30-81) and that of the case group was  $56.22 \pm 13.88$  (R=30-90). The rate of GI cancers in men was 1.5 times that of women.

Both the case and control groups had almost similar distributions of age, sex, and marital status, and no significant difference was observed between them ( $p > 0.05$ ). Yet, the two groups were significantly different in terms of education, occupation, family history of cancer, opium, cigarette and hookah smoking ( $p < 0.001$ ). The case group had more education than the control. Most participants in the case group were farmers. Most of the control group were employees. 26.7% of the case group and 6.7% of the control reported a family history of cancer. The prevalence of opium, cigarette, and hookah consumption in the case group was 55%, 40%, and 65%, respectively. This rate in

the control group was 4.2%, 10%, and 9.2%, respectively, and this difference was statistically significant ( $p < 0.001$ ) (Table 1).

Table 1: Characteristics of patients with GI cancer (case) and control

Variable	Variable level	Control(n=120)	Case(n=60)	P-value
		f (%)	f (%)	
Age	30-50	48(40.0)	23(38.3)	0.83
	>50	72(60.0)	37(61.7)	
Sex	male	74(61.7)	36(60.0)	0.83
	female	46(38.3)	24(40.0)	
Marital status	married	120(100.0)	58(96.7)	0.11
	single	0(0.0)	2(3.3)	
Educational Level (Years)	<6	20(16.7)	3(5.0)	<0.001
	6-12	49(40.8)	6(10.0)	
	>12	51(42.5)	51(85.0)	
Occupation	CLERC	45(37.5)	1(1.7)	<0.001
	Housewife	20(16.7)	14(23.3)	
	Farmer	20(16.7)	36(60.0)	
	Other	35(29.2)	9(15.0)	
Family History of Cancer	yes	8(6.7)	16(26.7)	<0.001
	no	112(93.3)	44(73.3)	
Opium use	ever	5(4.2)	33(55.0)	<0.001
	never	115(95.8)	27(45.0)	
cigarettes	ever	12(10.0)	24(40.0)	<0.001
	never	108(90.0)	36(60.0)	
Hookah use	ever	11(9.2)	39(65.0)	<0.001
	never	109(90.8)	21(35.0)	

The results summarized in Table 2 show that after controlling potential confounders (age, sex, education level, occupation, and family history of cancer), opium and hookah consumption were significantly correlated with GI cancers ( $p\text{-value} < 0.05$ ). However, smoking was not significantly correlated with GI cancers ( $p = 0.27$ ).

Table 2: Risk Assessment of GI Cancers, represented by Odds Ratio (OR) and 95% Confidence Interval (CI), Case–Control Study

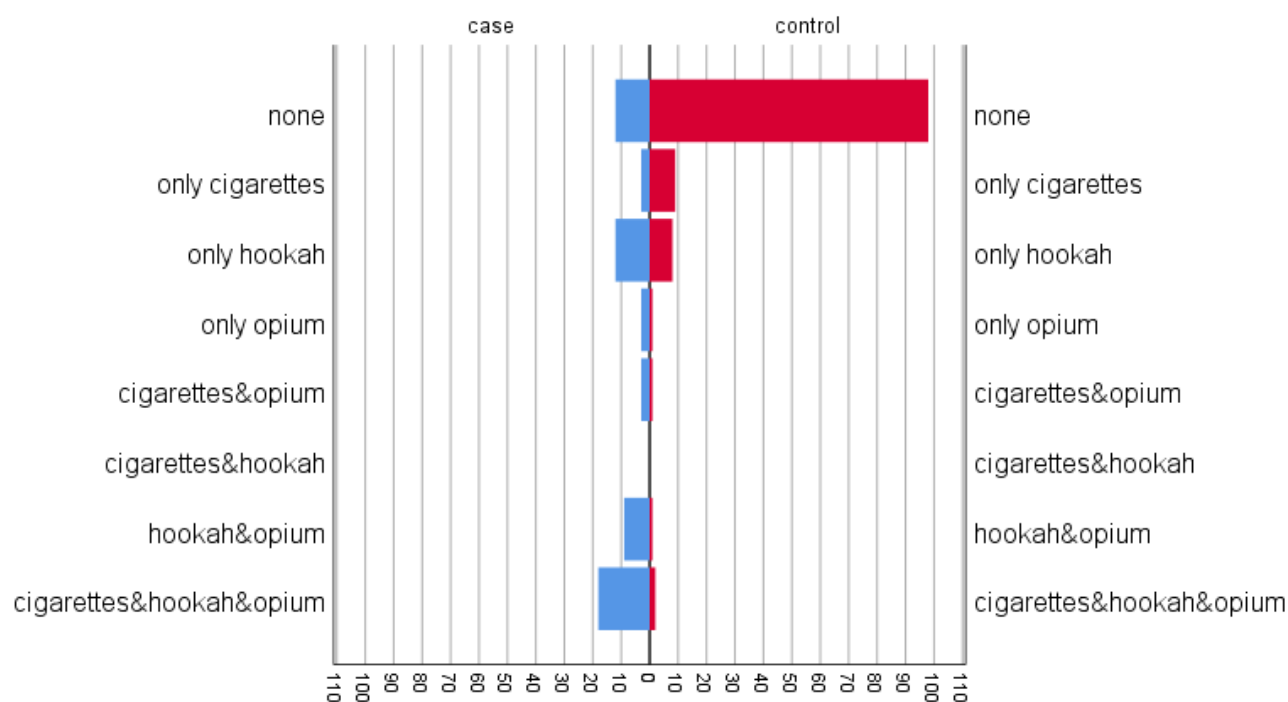


	OR crude (95%CI)	p-value	OR adjusted (95%CI)	p-value
Age(>50 vs 30-50)	1.07(.57-2.02)	0.83	.07(.01-.34)	0.001
SEX(female vs male)	1.07(.57-2.02)	0.83	.71(.15-3.33)	0.67
Education Level (Years)				
6-12	.82(.18-3.59)	0.79	1.62(.07-35.71)	0.76
>12	6.67(1.86-23.83)	0.004	13.12(.46-375.77)	0.13
Occupation (CLERC)				
Housewife	31.50(3.87-256.21)	0.001	14.41(9.93-223.37)	0.06
Farmer	81.00(10.37-632.75)	0.000	24.41(2.06-289.38)	0.01
Others	11.57(1.39-95.70)	0.02	3.02(.20-44.72)	0.42
Family History of Cancer	5.09(2.03-12.74)	0.001	5.04(1.17-21.62)	0.03
Opium use	30.08(10.73-84.31)	0.000	5.81(1.17-28.81)	0.03
Cigarettes use	6.00(2.73-13.21)	0.000	2.55(.49-13.29)	0.27
Hookah use	18.40(8.14-41.62)	0.000	8.29(2.39-28.77)	0.001

Table 3: Logistic regression for the risk ratio of gastrointestinal cancers related to the simultaneous use of tobacco and opium

	OR*	95% C.I for OR		p-value
		lower	upper	
Tobacco and Opium				
Non(Ref)	-	-	-	0.000
Only cigarettes	5.08	0.86	29.81	0.07
Only Hookah	17.71	4.72	66.43	0.001
Only Opium	31.05	2.43	396.55	0.008
Cigarettes & opium	77.08	4.20	1413.08	0.003
Hookah & opium	65.81	6.17	701.69	0.001
Cigarettes & hookah & opium	110.74	16.07	763.32	0.001

\*Odds Ratio for GI after adjusted for sex, age, education, job, and family cancer



*Figure 1. Distribution of tobacco and opium consumption in the case and control groups*

The exclusive use of tobacco and opium (i.e., each on its own) showed to greatly increase the risk of GI cancers. This risk significantly increased, respectively, in people smoking only cigarettes (OR=5.08), only hookah (OR=17.71), only opium (OR=31.05), both opium and hookah (OR=65.81), both opium and cigarettes (OR=77.08) and all three together (cigarettes, hookah and opium) (OR=110.74). The OR in all groups ( $p < 0.05$ ) was statistically significant except in those only smoking cigarettes ( $p = 0.07$ ) (Table 3).

## Discussion

The present study tested the relationship between hookah and opium smoking and the effects of their simultaneous use on GI cancer in Minab, a city in Hormozgan province. The results showed a positive and significant relationship between opium and tobacco use and GI cancers. The results of cohort studies conducted in high-risk areas of GI cancers in Iran such as Golestan and Ardabil (19) show that opium and tobacco, especially hookah, are a



risk factor for these cancers (17, 19, 20). Compared to other parts of Iran, Hormozgan province in the south of Iran is considered a low-risk area for GI cancers with a low incidence of these cancers (21). However, the incidence rate along several years shows that the increased incidence of these cancers in recent years(22), and the increased exposure to risk factors such as opium and tobacco use, especially hookah in Hormozgan province (23, 24) can increase the importance of the issue.

The present findings showed that smoking opium and tobacco (hookah and cigarettes) each on its own and their simultaneous use significantly increase the risk of GI cancers. These results are consistent but significantly stronger than the results of previous studies. In Golestan cohort study, the risk of ESCC (esophageal squamous cell carcinoma) was higher in those smoking tobacco and opium both (OR=2.35, 95% CI=1.50-3.67) than those only smoking opium (OR=2.12,95% CI: 1.21-3.74) (25). In the present study, the prevalence of GI cancers in men was 1.5 times that of women. However, in Golestan cohort study, this rate was the same. As in the present study, the prevalence of opium and tobacco use is higher in men, this finding can be justified.

Opium consumption is associated with the increased risk of GI cancers (3), including esophagus (26), pancreatic cancer (15, 25, 26), stomach (15, 17, 26), colon (26), liver cancer (15) and colorectal cancer (28). However, in recent studies, researchers did not find evidence for carcinogenicity of raw opium in animal and human studies (29). However, illegal opium products (latex, burnt, raw or crude opium), especially opium pyrolysis (burnt), contain secondary pollutants and impure Substances and are intoxicated with heavy metals, including some known carcinogens such as lead, arsenic, chromium, cadmium (27). In addition to opium, hookah consumption was another risk factor of GI cancers in the present study. These results are in line with the results of Ardabil cohort study, in which hookah use was found to be a risk factor for stomach cancer and precancerous lesions. In our study, although smoking only increased the risk of GI cancers, this risk was not significant (OR=5.08, CI=0.86-29.81). This is in line with the results of a study in Shiraz showing that smoking is associated with cancers of the lower GI tract (OR 1.01; 95% CI: 0.59-1.78) (28). Also, in another study, no significant relationship was found between smoking and the risk of pancreatic cancer (OR 0.93; 95% CI 0.62-1.39) (25).

Studies show that smoking causes various chronic inflammatory diseases of the digestive system. Chronic inflammation can induce tumorigenesis through the induction of genomic instability, which leads to mutagenesis (31). Cigarette smoke contains a wide range of toxic and carcinogenic components such as aromatic amines, phenolic compounds, alkaloids, PAHs, TNSA, and heavy metals. Nicotine, as the most active component of cigarette smoke, plays an important role in gastric ulcers and Crohn's disease, and as a result, the development of cancer in esophagus,

stomach, colon, and liver (32). Evidence shows that hookah smokers are exposed to many of the same toxic compounds as cigarette smokers, but at much higher levels that may lead to more severe adverse effects on health. In fact, hookah smokers are at risk of infection, cancer, lung disease and other diseases (33). A secondary finding of this study was that the prevalence of GI cancers was higher in farmers and then in housewives (most likely wives of farmers). Minab is the largest agricultural center in the south of Iran. Unfortunately, the high consumption of industrial poisons and fertilizers in this city further justifies this result. There is a need for more detailed investigations.

### **Limitations, Strengths and future research:**

The present study showed the relationship between opium and tobacco use and the cumulative effects of their simultaneous use in developing GI cancers in the south of Iran, faced with a significant dearth of research on the topic. The present findings can motivate the replication of study with a larger sample for other researchers. One major challenge in tobacco and opium studies is the collection of reliable consumption data and the fear of stigma and legal prosecution (15). Also, patients may have used opium and its derivatives to control pain. In almost any case, it causes potential biases in collecting information and underestimating or overestimating the risk. Therefore, we considered Substance abuse in patients before the diagnosis of disease and excluded those who began consuming Substances after the diagnosis of disease.

Another challenge was that, although all available patients were included in the study, the number of patients was lower than other studies and nothing could be done about it. One limitation of other studies was not knowing the type of opium product consumed, the amount and duration, and the unit of opium and tobacco consumption. Since cancer is a multifactorial disease (27), failure to adjust for other known risk factors such as consumption of hot foods, *Helicobacter pylori*, alcohol consumption, food consumption, consumption of nitrates and toxins (17, 25, 35) can threaten the homogeneity of risk assessment. However, it is recommended that researchers minimize these confounding factors.

### **Conclusion**

This study revealed a significant and positive relationship between opium and tobacco use and GI cancers. The risk of these cancers increased significantly in patients who smoked both tobacco and opium. Considering that

cancer prevention is the most affordable strategy in controlling this disease, the findings of this study will help prevent this disease through identifying some risk factors of GI cancers. It is recommended to design comprehensive studies considering the pattern of Substance Abuse, and design studies to understand the role of each Substance and its effects for preventive purposes.

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## Authors' contribution

Conceptualization: Maryam Karimi Jaberi  
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## Competing interests

The authors declare that there are no conflicts of interest.

## Ethical issues

The study protocols were approved by the Ethics Committee of Hormozgan University of Medical Sciences, Bandar Abbass, Iran (Ethical code:IR.HUMS.REC.1397.171).

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