Introduction
Smoke from the burning of tobacco contains more than 4000 hazardous components. Many of these items turned out to be harmful to the respiratory mucosa (1). Smoking is one of the leading causes of death and illness around the globe, particularly in underdeveloped nations (2). There are over 1.1 billion smokers worldwide, and the World Health Organization estimates that half of them die yearly (2). Smoking may harm many different body parts, including the nose and sinuses. In this regard, the current study sought to gather information to analyze the link between smoking and sinonasal disorders.

Evidence Acquisition
Several databases such as PubMed, Scopus, Web of Sciences, and Google Scholar were searched for related articles published from inception until 2021. Of the overall 560 retrieved articles, 67 cases remained for review after the exclusion of duplicates and unrelated papers. Tobacco smoke, whether first- or second-hand, is harmful to the nose and sinuses. Smoking is linked to various sinonasal disorders, including chronic rhinosinusitis (CRS), olfactory impairment, nasal polyps, allergic and non-allergic rhinitis, and certain cancers. The formation of bacterial biofilms, dysfunctional mucociliary clearance, oxidative stress, inflammation, apoptosis, and cytotoxicity, and structural changes appear to be some of the potential mechanisms through which tobacco smoke affects the sinuses and the nose. Clinicians should consider the negative consequences of smoking on sinonasal disorders when treating patients with these conditions. Cessation of smoking may benefit these patients’ health.

Keywords: Smoking, Tobacco, Sinus, Nose, Sinonasal disease

Results
The Potential Processes Through Which Smoking Can Harm the Nose and the Sinuses
Bacterial Biofilms
More evidence points to the possibility that smoking cigarettes stimulates the growth of biofilms in a range of pathogenic bacteria (3, 4). Bacterial biofilms include cells that are encased in a self-produced polysaccharide matrix and vary from other bacteria in terms of their genotype and phenotype (5, 6). Because of the increased antibiotic resistance brought on by tobacco use, tobacco-induced biofilm development may be a factor in the refractory character of many respiratory disorders observed in smokers and passive smokers (5). Consistently, nasal biofilms may form in children who are exposed to passive smoking at home and those who may be more susceptible to recurring sinus infections and other respiratory diseases (7).
hookah, have also been shown to impair mucociliary clearance (13). Additionally, cigarette smoke reduces the ciliogenesis of respiratory cells, which may also affect mucociliary clearance (14).

Smoking tobacco has been associated with altered mucus secretion mechanisms and an increase in the quantity and size of glandular cells (15). Further, smoking could reduce the frequency of ciliary beats and retard the ciliary regeneration of nasal mucosa after sinus surgery (16, 17). On the other hand, cotinine, a hazardous byproduct of nicotine, was reported by Agius et al to drastically lower the ciliary beat frequency in vitro (18). Following in vitro exposures to cigarette smoke, the reduction of chloride transport was observed in epithelial cells, which is comparable to what occurs in people with cystic fibrosis (19, 20).

**Oxidative Stress**

Several reactive oxygen species (ROS), including the superoxide anion, hydrogen peroxide, and the hydroxyl radical, cause oxidative damage to proteins, DNA, and lipids in the respiratory epithelium (21). The respiratory tract is considered to be particularly susceptible to oxidative damage due to its prolonged exposure to high amounts of oxygen, as well as its rich blood supply and wide surface area (22, 23). Tobacco smoke contains millions of free radicals in a single puff. As a result of the high concentration of these components, smoking cigarettes is a well-established external trigger for inflammation (24). In the presence of water, airborne smoke rapidly degrades, releasing high quantities of ROS (25). Moreover, cigarette smoke exposure inhibits cell migration and collagen contraction activity in nasal fibroblasts through the ROS/AMPK signaling pathway (26).

**Inflammation**

Cigarette smoking is a potent pro-inflammatory stimulant that has been associated with the activation of an intricate inflammatory response that results in the creation of a wide range of strong chemokines and cytokines, disrupting the balance of pro- and anti-inflammatory cytokines (27, 28). Smokers’ sputum, compared to that of non-smokers, contains higher levels of mononuclear cells, and their serum contains higher amounts of cytokines such as interleukin 6, interleukin 8, and tumor necrosis factor-alpha. There are, however, few investigations on the distinctions between systemic and local inflammatory behavior in smokers (29-31). Nevertheless, Berania et al demonstrated elevated levels of systemic inflammation markers in chronic rhinosinusitis (CRS) patients who smoked actively (32).

**Apoptosis and Cytotoxicity**

In vitro studies represented that the growth of primary nasal epithelial cells depends on the vascular endothelial growth factor (VEGF) and that cigarette smoke exposure impairs cell growth and promotes apoptosis of these epithelial cells. The effects of cigarette smoke exposure might be mediated through VEGF-dependent pathways (33). Furthermore, smoking causes the sugars in tobacco to burn, resulting in the byproduct of acrolein. Primary nasal epithelial cell cultures are stimulated and immunosuppressed by acrolein and nicotine, respectively, when employed at quantities relevant to smokers’ airways, suggesting cytotoxicity (34).

**Structural Changes**

A large cross-sectional study on 2523 patients referred for chronic nasal complaints conclusively revealed that smokers have lower minimal cross-sectional area, nasal cavity volume, and peak nasal inspiratory flow than non-smokers (35).

**Smoking-associated Sinonasal Diseases**

**Chronic Rhinosinusitis**

The incidence of CRS has been strongly linked to active smoking in previous population-based research, with a probable dose-dependent relationship (36, 37). Additionally, a recent systematic review indicated a higher frequency of CRS among smokers (38). However, some studies reported no significant connection in this regard (39, 40). In a study by Huston et al, although smoking prevalence did not differ between patients with CRS and individuals without CRS, CRS symptoms were associated with smoking (41). Similarly, Wolf et al found that active and passive smoking were strongly associated with the severity of CRS symptoms (42). In a systematic review, second-hand smoke was also associated with sinusitis (43).

**Olfactory Dysfunction**

Previous studies suggested that smoking is one of the leading causes of olfactory impairment (44, 45). Squamous metaplasia and altered shape of olfactory receptor neurons have been discovered during the histological analyses of smokers’ olfactory epithelium (46), which has been confirmed in animal studies (47, 48). The olfactory function is about equally affected by passive smoking (49).

**Nasal Polyps**

They are nasal mucosa outpouchings histologically characterized by edematous stroma, epithelial remodeling, and various inflammatory cellular infiltrates. Although the literature reveals numerous causes, the etiology of nasal polyposis is not entirely understood yet (50). Epithelial remodeling is a key feature of airway disorders and includes goblet cell hyperplasia, squamous metaplasia, and epithelial hyperplasia (51, 52). Gao et al demonstrated a substantial correlation between smoking and squamous metaplasia in nasal polyposis (53). In
addition, another research indicated that cigarette use is linked to an increased incidence of nasal polyposis (54). On the other hand, changes in the immune response caused by tobacco smoke in the sinonasal epithelium may be a critical factor in the development of CRS with nasal polypos (55). Conversely, according to Kule et al, although smoking is connected with histological alterations in the respiratory mucosa, no significant differences were discovered in the histopathological features of nasal polypos among smokers (56).

Allergic and Non-allergic Rhinitis
Unlike non-smokers, smokers with allergic rhinitis had greater leukotriene B4 levels and lower P in exhaled breath condensate, which may make these patients more vulnerable to the harmful effects of smoking (57). Moreover, compared to allergic rhinitis patients who had not been exposed to second-hand smoke, allergic subjects, who had been exposed to this type of smoke, were more likely to use nasal decongestants and report more severe nasal symptoms such as nasal blockage and discharge (58). Nevertheless, in a study on 4339 adult subjects, tobacco smoke exposure was related to an increase in the incidence of rhinitis symptoms but not allergic sensitization (59). On the other hand, it has been suggested that smoking is a major pathogenic cause of non-allergic rhinitis (60). Håkansson et al also proposed smoking as a significant modulator of non-allergic rhinitis (61).

Malignancies
Inverted papilloma is one of the most prevalent sinonasal tumors. The malignant transformation of sinonasal inverted papilloma is linked to a smoking history (62). Likewise, the recurrence of inverted papilloma following surgical excision seems to be connected to smoking (63). Moreover, tobacco use has been associated with an increased risk of sinonasal cancer, particularly the squamous cell subtype (64-66). Conversely, a recent review suggested no significant relationship between smoking and the development of sinonasal malignancies unlike other head and neck cancers (67).

Conclusion
First- or second-hand tobacco smoke has detrimental effects on the nose and sinuses. Smoking has a role in many sinonasal disorders, including CRS, olfactory dysfunction, nasal polyps, allergic and non-allergic rhinitis, and some tumors. Bacterial biofilm formation, dysfunctional mucociliary clearance, oxidative stress, inflammation, apoptosis and cytotoxicity, and structural changes appear to be some potential mechanisms through which tobacco smoke affects the sinuses and the nose.

Conflict of Interest Disclosures
None.

Ethical Statement
Not applicable.

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