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Systematic Review

Divergent prevalence of Warthin tumor in Africa and Asia: A consequence of variation in smoking index?

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Abstract

Aim: This study assessed the prevalence of WT in Africa and Asia as it relates to smoking index and malignant tumors of the parotid gland.

Materials and Methods: Peer-reviewed articles found on Google Scholar, Scopus, EMBASE, Web of Science, and PubMed Central were systematically reviewed.

Results: Significant higher prevalence of WT and smoking index (intensity and prevalence of smoking) were observed in Asia than in Africa (p= 0.003 and p=0.001, respectively). A significant direct relationship was observed between the frequency of WT and smoking index (p= 0.001) while a significant inverse relationship between the prevalence of WT and malignant tumors of the parotid gland (p= 0.039) was also observed. In Africa, South Africa and Morocco had the highest prevalence of WT (13.4% and 11.5%, respectively) while Tanzania and Nigeria had the lowest prevalence of WT (3.6% and 0.0%, respectively). In Asia, Taiwan and South Korea had the highest prevalence of WT (46.6% and 38.8%, respectively) while Iran and Pakistan had the lowest prevalence of WT (7.6% and 3.5%, respectively).

Conclusion: This review revealed that the high prevalence of WT in Asia could be due to a high smoking index in the continent. It suggests that the incidence of WT could be used as an alternative tool for monitoring the effect of smoking across countries.

Keywords: Africa; Asia; smoking index; Turkey; warthin tumor

INTRODUCTION

The salivary glands, which majorly consist of the parotid, submandibular and sublingual glands, are affected by a variety of lesions ranging from inflammation (24.4%) to neoplasia (73.1%) (1). Benign tumors of salivary glands predominantly include pleomorphic adenoma, Warthin's tumor (WT), and oncocytoma while common malignant tumors include squamous cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, and acinic cell carcinoma (2,3). Warthin's tumor, also known as adenolymphoma or papillary lymphomatous cystadenoma, is the second most common benign neoplasm of the parotid gland, comprising 2-15% of the parotid epithelial tumors and approximately 5-6 % of epithelial salivary gland neoplasms (2,4). It is a slow-growing mass with epithelial, glandular, and lymphoid histological characteristics (4,5). The tumor is commonly localized in parotid gland cauda and rarely in peri-parotid lymph nodes (8%) (6). Evidence suggests that smokers, especially those who are between the ages of 40 to 71 years, are 8 times at risk of developing WT than non-smokers (7,8). Of note, 32.2% of adolescents in Africa have smoked cigarettes at one point in their lives while 20.8% are current smokers (9). Additionally, accumulation of aged mitochondria following the deletion of 4977-bp in the mitochondrial genome and progressive loss of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) has also been linked to WT tumorigenesis (10,11). Other risk factors for WT which have also been implicated in malignancy include high body mass index and triglyceride, and exposure to plastic and painting materials (12,13). Despite the consistent decrease in cigarette smoking in countries with stable and strong economies such as Germany, Poland, and Japan (14), the prevalence of WT is consistently increasing. In Germany, Franzen et al. reported a decade-wise increase in the incidence of WT from 20.6% (in 1975) to 44.9% (in 2017) (15). In Austria, Kadletz et al. also observed a substantial increase in WT from 9.1% (in 1960) to 60.6% (in 2015) (12). Interestingly, the prevalence of WT is higher in Caucasians than in African-Americans (29.6% vs 4.08%, respectively) (16). However, there is a paucity of data on the trend of WT incidence in Africa and Asia. Thus this review compared the prevalence of WT in Asia and Africa in relation to cigarette consumption

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and malignancy of the parotid gland. It also revealed the periodic differences in the prevalence of WT between Turkey and other countries.

MATERIALS and METHODS

Published peer-reviewed articles (full text) found on databases such as Google Scholar, Scopus, Web of Science, and PubMed (central) were selected and reviewed using the PRISMA standard (Figure 1). Only studies which histologically classified tumors and/or studies that used the Milan System for Reporting Salivary Gland Cytopathology were included in this study. The data generated were analyzed and presented as descriptive statistics (Table 1). T-test was used to compare the prevalence of WT, and smoking index (intensity and prevalence of smoking) in Africa and Asia. The smoking index in countries (lower and upper limits) was graded on a scale of 1 to 6: Low consumption of cigarettes by smoker/day (1 and 2), medium consumption (3 and 4) and high consumption of cigarette by smoker/day (5 and 6) (17). Pearson's correlation was used to correlate the prevalence of WT in the parotid, and smoking index. Tunc et al. stated the yearly prevalence of WT in Gaziantep (Turkey) from 2000-2019 (18). In other to show the periodic differences between Turkey and other countries, Gaziantep was used as the reference study.

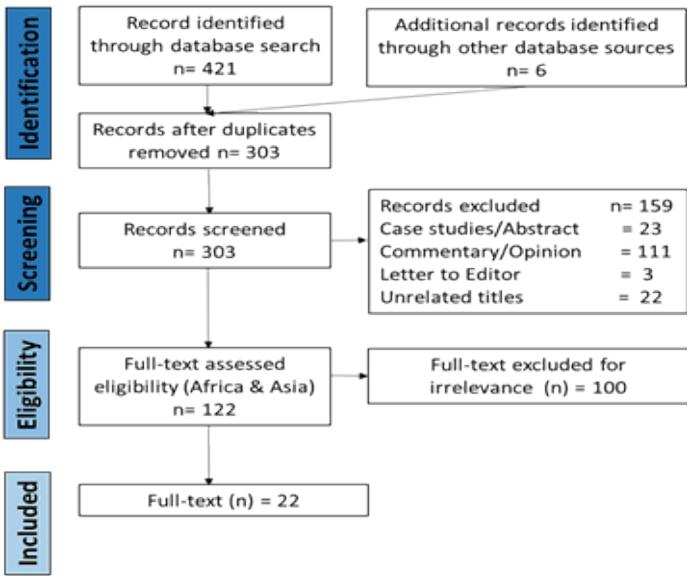

Figure 1. PRISMA flow diagram on literature search for benign and malignant tumors

RESULTS

A significant direct relationship was observed between the frequency of WT in benign parotid gland tumors and smoking index (r= 0.665, p= 0.001). Significant higher

Table 1. Prevalence of WT among benign parotid gland tumors in Asia and Africa

Country [Smoking index (17)]	B/M ratio	WT/B (%)	Period of study	Trend of WT/B (%) in Turkey	Year/(Reference)
Asia					
Turkey (4)	4.8:1	33.1	1984-2019		(6,18-22)
Turkey **(Gaziantep)**	12.6:1	38.1	2000-2019	**Reference timeline**	Tunc et al. (18)
Turkey (Adana)	5.8:1	38.6	2011-2016	↓30.3	Yazici et al. (19)
Turkey (Istanbul)	4.7:1	30.6	2008-2015	↓27.1	Comoglu et al. (20)
Turkey (Ankara)	3.7:1	30.8	1984-2012	-	Kizil et al. (6)
Turkey (Manisa)	4.3:1	21.9	2000-2009	↑24.0	Derin et al. (21)
Turkey (Izmir)	2.3:1	18.2	1994-2005	-	Etiti et al. (22)
Malaysia (4)	10.2:1	37.3	2014-2018	↓34.8	Rahman et al. (23)
Kingdom of Saudi Arabia (KSA; 5)	3.3:1	36.8	2014-2018	↓34.8	Fatima et al. (24)
Iran (5)	1:1.1	7.6	2005-2015	↑26.8	Taghavi et al. (25)
South Korea (6)	6.4:1	38.8	2010-2013	↓30.6	Lee et al. (26)
China (6)	3.5:1	26.6	1963-2012	-	Gao et al. (27)
Japan (6)	6.2:1	34.6	1973-2011	-	Sentani et al. (28)
Nepal (2)	1:1.6	15.4	2005-2010	↑21.6	Shrestha et al. (29)
Pakistan (3)	9.5:1	3.5	2003-2010	↑22.0	Shah et al. (30)
Taiwan (5)	7.0:1	46.6	2002-2010	↓24.6	Liao et al. (31)
Africa					
Ghana (3)	1.7:1	6.6	2009-2016	↑29.0	Titiloye et al. (32)
Niger (1)	6.1:1	9.3	2010-2014	↑27.8	Ille et al. (33)
Nigeria (3)	5.9:1	0.0	2007-2014	↑24.3	Onotai et al. (34)
Senegal (1)	2.1:1	11.1	2000-2012	↑26.1	Bouaity et al. (35)
Morocco (3)	4.0:1	11.5	1992-2007	-	Diom et al. (36)
South Africa (3)	2.2:1	13.4	1994-2004	-	van Lierop et al. (37)
Tanzania (1)	1:1.1	3.8	1982-2001	-	Masanja et al. (38)

Keys: B= Benign tumor, M= Malignant tumor, WT= Warthin tumor, S.I.= Smoking index

prevalence of WT and smoking index were observed in Asia than in Africa (Figure 2) while an insignificant higher prevalence of malignant parotid tumors was observed in Africa than in Asia (p= 0.496). A significant inverse relationship was observed between the prevalence of WT and malignancy of the parotid gland (Figure 3; r= -0.433, p= 0.039). Table 1 shows a substantial increase in the prevalence of WT in Asia, particularly in Turkey. However, no increase in the prevalence of WT was observed in Africa.

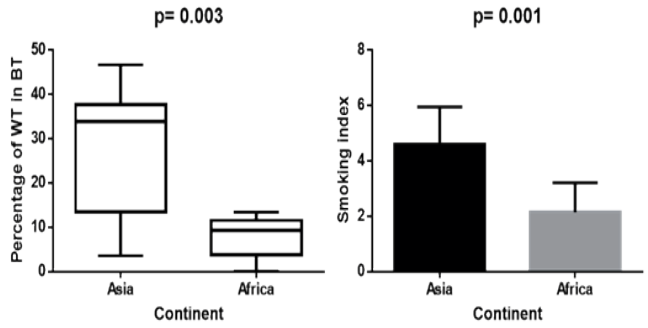

Figure 2. Frequency comparison of WT (Table 1) and smoking index (17) between Africa and Asia

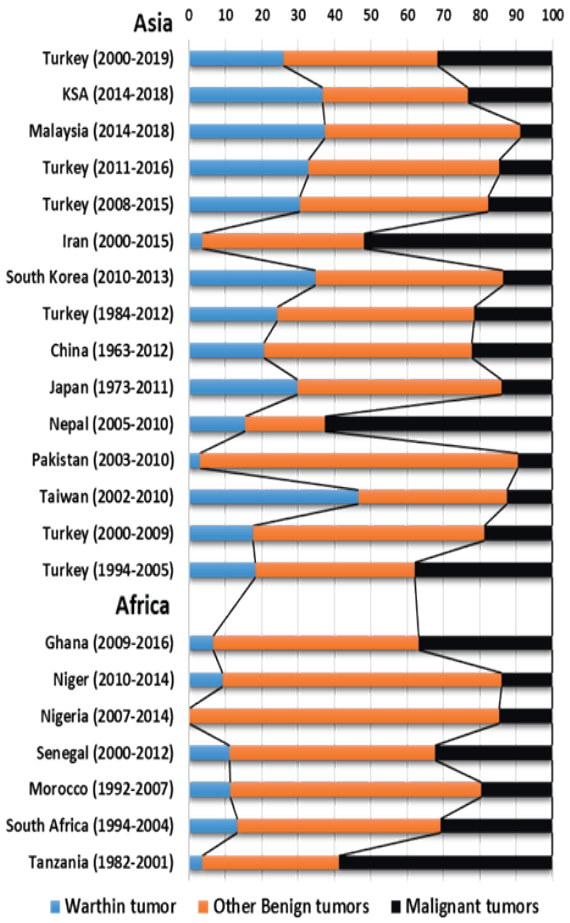

Figure 3. Country-based prevalence of WT, other benign tumors and malignant tumors of the parotid gland (6,18-38)

DISCUSSION

According to Ng et al., smokers in Africa consume ≤15 cigarettes per day while smokers in Asia consume ≥20 cigarettes per day (17). The variation in the rate of smoking between Asia and Africa could be due to differences in climatic conditions. Studies have shown that individuals who smoke more than 10 cigarettes/day and have been smoking for over 20 years are at a higher risk of developing neoplastic tumors (4,12). Thus, low cigarette smoking could be associated with the low prevalence of WT in most African countries while the high prevalence of WT could be adduced to the medium to the high prevalence of smoking in Asia (17,39). Since current smokers are at a higher risk of developing WT than past smokers when compared with non-smokers (37 times vs 4 times, respectively) (40), the low prevalence of WT in Iran and Pakistan, despite the high prevalence of WT in other Asian countries, could be due to reduced consumption of cigarette. The proximity of Iran, and Pakistan to Africa also implicates climatic conditions and/or geographical location as a possible indirect inhibitor(s) to WT tumorigenesis. On the other hand, the low prevalence of WT in Africa, Iran and Pakistan maybe due to low genetic mutation.

The decade-wise increase in WT prevalence in Turkey from 24.0% (in 2000-2009) to 38.1% (2010-2019) may be due to the increasing consumption of cigarettes (18). This is underscored by the fact that the number of smokers among patients diagnosed with WT increased from 82.7% (in 2009) to 92% (in 2019) (18,21). Considering the period in which studies were carried out in Turkey, the prevalence of WT in Gaziantep was higher than that of Manisa but lower than that of Adana and Istanbul. More so, considering the period in which patients were investigated in Asia and Africa, the prevalence of WT in Gaziantep was also higher than that of Iran, Nepal, Pakistan, Ghana, Niger, Nigeria, and Senegal but lower than that of Malaysia, KSA, South Korea, and Taiwan. Since the prevalence of WT is increasing yearly, the prevalence of WT in Adana and Istanbul (Turkey), Malaysia, KSA, South Korea, and Taiwan may be greater than 38.1% (in 2019) among histologically diagnosed benign tumors of the parotid gland. Interestingly, some countries with a low prevalence of WT, especially Nepal, Iran and Tanzania had a higher prevalence of malignant tumors of the parotid gland than regions with a high prevalence of WT. The reason for this is still unknown. Thus, further studies are warranted.

CONCLUSION

This review revealed that the difference in the prevalence of WT between Asia than in Africa could be due to extent of cigarette consumption. It suggests that the prevalence of WT could be used to assess the paradigm shifts in smoking index. Screening individuals who smoke greater than 10 cigarette/day over a period of 20 years may aid early detection of WT.

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