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Original Study

# Mobile Phone Use and the Risk of Parotid Gland Tumors: A Retrospective Case–Control Study

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## Abstract

### Background

Mobile phones are integral part of the modern lifestyle. As they emit radio frequency electromagnetic field, their role in carcinogenesis needs to be ascertained. The goal of this study was to investigate the association between the use of cellular phones and the risk for parotid gland tumors.

### Materials and Methods

A total of 26 patients diagnosed with parotid gland tumors and 61 healthy controls were enrolled through a hospital–based retrospective case–control study. The patients were referred and admitted to a tertiary hospital from January 1996 to March 2013.

### Results

The Odds of exposure were 3.47 times higher among patients compared to their controls. 95% CI suggested that the true Odds Ratio (OR) at the population level could be somewhere between 1.3 and 9.23 and so the observed OR was statistically significant at 5% level of significance.

### Conclusions

Overall, an association between the exposure of cellular phone use for more than 1 hour daily and parotid tumor was observed. This association should be interpreted with caution because of the relatively small sample size.

### Keywords

parotid gland tumor, mobile phone, non–ionizing radiation, risk factor, radiofrequency electromagnetic field

## استخدام الهواتف الجوالة واختطار الإصابة بأورام الغدة النكفية : دراسة استعادية للحالات والشواهد

### المحتوى:

أصبحت الهواتف الجوالة جزءً لا يتجزأ من نمط الحياة الحديثة. و لكونها مصدرا لانبعاثات المجال الكهرومغناطيسي ذات التردد الراديوي (اللاسلكي)، فقد دعت الحاجة للتأكد من كونها مسبب للتسرطن من عدمه . و قد هدفت هذه الدراسة للتحقق من مدى العلاقة بين استخدام الهواتف الخلوية واختطار الإصابة بأورام الغدة النكفية .

### المواد والطرق:

أجريت الدراسة على 26 مريض ممن تم تشخيص إصابتهم بأورام الغدة النكفية و 61 من الأفراد الشواهد ، والذين تم تسجيلهم في المستشفى كحالات خاضعة للدراسة الاستعادية للحالات والشواهد . وقد تم إحالة المرضى وتنويمهم في مستشفى جامعي في الفترة من شهر يناير 1996 وحتى شهر مارس لعام 2013.

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## النتائج:

كانت احتمالية التعرض بين المرضى تعادل 3،47 مرة بين الشواهد . و قد اقترح أن 95% بالنسبة لـ CI أن نسبة الاحتمالية الصحيحة على مستوى السكان قد تكون ما بين 1.3 و 9.23 ، ولذلك فإن نسبة الاحتمالية الملحوظة كان معتد بها إحصائياً عند 5 % من مستوى الدلالة .

## الخلاصة:

بالرغم من صغر عدد العينة البشرية لهذه الدراسة ، إلا أنه لوحظ وجود ارتباط بين احتمالية التعرض للإصابة بورز الغدة النكفية و استخدام الهاتف الخلوي لأكثر من ساعة يومياً .



## الكلمات الأساسية:

ورم الغدة النكفية – الهاتف الجوال – الإشعاع غير المؤين – عامل اختطار – الموجات اللاسلكية في المجال الكهرومغناطيسي ذات التردد اللاسلكي .


## Introduction

With the emergence of new digital telecommunication technologies, the use of mobile phones have become increasingly an indispensable part of our daily life. Global mobile subscriptions reached an estimated 6.8 billion at the end of the 2013(ITU, International Telecommunication Union, Barcelona, 7 October 2013). According to the database of ITU World Telecommunication /ICT Indicators, in 2013 the number of mobile phone use per hundred people is 96.2 % globally, the number exceeding 200 in some countries.

The fact that mobile phones have become ubiquitous warrants concern about its effect on the health of the users[1–4]. Radiofrequency electromagnetic fields (radio waves) are emitted from mobile phones during communication, which operates within the frequency range of 450 and 2700 Mhz. Health hazards associated with the exposure to this radiofrequency electromagnetic fields cannot be totally ruled out and needs to be investigated. The ionizing radiation has been correlated with different cancers1and is a well–established risk factor for inducing carcinogenesis in salivary gland[5]. Although radiofrequency electromagnetic field is a non–ionizing radiation, it is categorized under Group 2 by the IARC (International Agency for Research on Cancer), meaning it is possibly carcinogenic to humans. Considering this fact and the anatomical proximity of the parotid gland to ear, possible association of mobile phone to parotid gland tumor cannot be completely eliminated. As the anatomical location of the parotid gland is in an area prone to the exposure to microwaves from cellular phones, research is focusing on its correlation with cancer[6]. Bearing this major health hazard in mind, measures can be taken for the prevention of such cancers.

Previous studies have suggested the possible health effects involved in the use of cellular phones, of which several have assessed correlations with parotid gland tumors[6–8]. The aim of this study was to investigate the relationship between the use of cellular phones and the risk for parotid gland tumors in an attempt to determine the potential association through a case–control hospital–based study.

## Materials and Methods

A hospital based study was carried out through a retrospective analysis of patients who have histopathologically confirmed parotid gland tumor. The patients were referred and admitted to a tertiary hospital from January 1996 to March 2013. Controls were recruited from the patients who attended the same hospital during the same time period for problem unrelated to parotid gland pathology, without any evidence of parotid gland disease or history of it. Informed consent was obtained from both cases and controls to get enrolled in this study. The study was approved by the institutional review board of King Saud University, KSA.

All participants were interviewed by the researchers using a unified questionnaire. The cases were reached by phone while the controls were interviewed directly during their clinic visits. Demographic characteristics matching were maximized between the two groups. Information on the total phone usage time per day,

years of using mobile phone, preferred ear while using cellular phone and mobile phone's brand name were recorded. Smoking status was also inquired as a confounding factor.

### Exposure

The exposure of study subjects were classified into two groups exposed and unexposed. Participants who reported daily cellular phone use of 1 hour or less were considered as unexposed, and those who reported daily use of more than 1 hour as exposed. Two time periods of cell phone use, less than 10 years and 10 years or more were used to analyze the latency time. The exposure was also calculated according to dominant ear used to listen.

### Data analysis

Odds Ratio (OR) estimated using logistic regression was used as the measure of association between the exposure and the disease, parotid tumor. Statistical significance of the OR at 5% level of significance was judged from the 95% Confidence Interval (CI) of OR. OR was judged to be statistically significant, if its CI did not include the value of 1, the value of OR under the null hypothesis of no difference. Crude ORs was estimated to measure the association of exposure and parotid tumor within subgroups. To control the effects of other factors like age of the participant, duration in years of mobile phone use, gender of the patient, brand of mobile phone, dominant ear used etc from that of the exposure, unconditional logistic regression was used. Chi–square test of association was used to test if the demographic profile of subjects is different between patients and control groups.

Ethical clearance was obtained from the institutional review board of King Saud University.

## Results

### Demographic and mobile phone usage profiles of control and patients groups

Initially 34 patients were enlisted in the study. Later 8 patients had to be excluded becausethe follow up data could not be obtained due to of wrong contact number in the hospital registry. Sixty one controls participated in this study. The demographic profile of both case and control is summarized in Table 1. About three quarters of cases were males compared to 44.3% in control group. The distribution of gender was not similar between patients and controls $\chi^2$ (1, 87) = 4.97, P = 0.026). While the majority of the control subjects were in the age group of <30 years (39.3%), the majority of the patients (34.6%) were in the age group of 50 years or more. The difference in the distribution of age between patients and controls were not large enough to be statistically significant $\chi^2$ (3, 87) = 5.67, (P = 0.129). While 68.9% of the controls used their right ear for attending the phone, patient predominantly (65.4%) used their left ear and difference in the pattern of predominant ear was statistically significant as tested using Chi–square test of association ($\chi^2$(2, 87) = 18.82, P < 0.001). The duration in years of use of mobile phone was similar among patient and control groups (Table 1). There was only one smoker in the entire sample and so smoking status could not be tested as independent variable in the analysis.

Among 61 controls, 24 (39.3%) were exposed to daily mobile phone use of more than one hour per day, while among the 26 patients, as many as 18 (69.2%) were exposed to daily mobile phone usage of more than one hour per day. As depicted in Table 2, the odds of exposure was 3.47 times higher among patients compared to their controls. 95% CI suggested that the true OR at the population level could be somewhere between 1.3 and 9.23,hence the observed OR was statistically significant at 5% level of significance (as the CI does not include 1.0 within its limits).

### Effect of age on the association of the exposure and parotid tumor

As noted earlier, there was some difference in the age distribution, though not statistically significant, between patients and controls. Hence, stratified analysis was carried out to control the effect of age of the participants. The OR, measuring the association between the exposure to daily use of mobile phone for more than 1 hour and parotid tumor, was 2.43 among study subjects in the younger age group of less than 30 years. But it was not statistically significant since its 95% CI, 0.28 to 20.82, contained the null value of 1. In the age group of 30–39 years, the OR was very high at 18 implying eighteen times higher risk for parotid tumor among the exposed group with statistical significance. But its 95% CI

| Characteristic | Control (n = 61) | Case (n = 26) | Total (n = 87) | $C^2$ (d.f) | P–value |
|---|---|---|---|---|---|
| Gender | 34 (55.7%) | 7 (26.9%) | 41 (47.1%) | 4.97 | 0.026 |
| Female | | | | (1) | |
| Male | 27 (44.3%) | 19 (73.1%) | 46 (52.9%) | | |
| Age of the participant | 24 (39.3%) | 4 (15.4%) | 28 (32.2%) | 5.67 | 0.129 |
| < 30 year | | | | (3) | |
| 30–39 years | 16 (26.2%) | 7 (26.9%) | 23 (26.4%) | | |
| 40–49 years | 9 (14.8%) | 6 (23.1%) | 15 (17.2%) | | |
| 50 years or more | 12 (19.7%) | 9 (34.6%) | 21 (24.1%) | | |
| Dominant ear used | 8 (13.1%) | 1 (3.8%) | 9 (10.3%) | 18.82 | < 0.001 |
| Both | | | | (2) | |
| Left | 11 (18%) | 17 (65.4%) | 28 (32.2%) | | |
| Right | 42 (68.9%) | 8 (30.8%) | 50 (57.5%) | | |
| Cell phone use | 33 (54.1%) | 14 (53.8%) | 47 (54%) | | |
| < 10 years | | | | 0.0 | 1.0 |
| | | | | (1) | |
| 10 or more years | 28 (45.9%) | 12 (46.2%) | 40 (46%) | | |
| Smoking | 61 (100%) | 25 (96.2%) | 86 (98.9%) | – | – |
| No | | | | | |
| Yes | 0 (0%) | 1 (3.8%) | 1 (1.1%) | | |
| | 37 (60.7%) | 8 (30.8%) | 45 (51.7%) | | |
| Cell phone use / day | | | | | 0.020 |
| ≤ 1 hr | | | | 5.38 | |
| | | | | (1) | |
| > 1 hr | 24 (39.3%) | 18 (69.2%) | 42 (48.3%) | | |

**Table 1. Comparison of demographic and cell phone usage profiles of control and case subjects**

ranged from 1.63 to 198.51 suggesting that the true value of OR in the population of 30–39 years old could be anywhere between 1.63 and 198.51. The very wide CI indicated imprecision of the OR, mainly due to inadequate sample size. The odds of exposure to daily use of mobile phone for more than 1 hour was 2.5 times among patients compared to their controls in the age group of 40–49 without statistical significance (95% CI: 0.29 to 21.4). The trend was in the opposite direction in the older age group of 50 years of more with an OR of 0.67 implying 33% less risk among the exposed group but the same was not large enough to be statistically significant since its 95% CI ranged from 0.10 to 4.48 (Table 2). Daily mobile phone use of more than 1 hour appear to be a statistically significant risk factor

| Characteristic | Ca/Co | OR | 95% CI |
|---|---|---|---|
| Overall (crude) | 18/24 | 3.47 | 1.30 to 9.23* |
| Age of the participant | 2/7 | 2.43 | 0.28 to 20.82 |
| < 30 year | | | |
| 30–39 years | 6/4 | 18.00 | 1.63 to 198.51* |
| 40–49 years | 4/4 | 2.50 | 0.29 to 21.4 |
| 50 years or more | 6/9 | .67 | 0.10 to 4.48 |
| Overall (adjusted for age) | 18/24 | 2.86 | 1.03 to 7.97* |
| Gender | 4/11 | 2.79 | 0.53 to 14.67 |
| Female | | | |
| Male | 14/13 | 3.02 | 0.85 to 10.74 |
| Overall (adjusted for gender) | 18/24 | 2.93 | 1.07 to 8.03* |
| Brand of cell phone | –/5 | – | – |
| Blackberry | | | |
| iPhone | 9/4 | 11.25 | 2.04 to 62.20* |
| Nokia | 7/11 | 1.59 | 0.24 to 10.57 |
| Samsung | 2/4 | 1.17 | 0.13 to 10.22 |
| Overall (adjusted for Brand). Blackberry users excluded. | 18/19 | 3.62 | 1.22 to 10.69* |
| Dominant ear used | 1/4 | – | – |
| Both | | | |
| Left | 10/4 | 2.50 | 0.52 to 11.93 |
| Right | 7/16 | 11.38 | 1.28 to 101.22* |
| Overall (adjusted for ear). Both ear users excluded | 17/20 | 4.65 | 1.41 to 15.37* |
| Cell phone use | 9/11 | 3.60 | 0.97 to 13.36 |
| < 10 years | | | |
| 10 or more years | 9/13 | 3.46 | 0.77 to 15.56 |
| Overall (adjusted for duration) | 18/24 | 3.54 | 1.32 to 9.51* |

**Table 2. Odds Ratio (OR) and 95% Confidence Interval estimates of association between the exposure of daily cell phone use of more than 1 hour and parotid tumor**

**Number of exposed cases (Ca) and controls (Co) given. Unconditional logistic regression was used to adjust OR for the differences of individual factors taken one at a time.**

*** statistically significant at p < .0**

| Site of tumor | Dominant ear while using phone | | | |
|---|---|---|---|---|
| | Both | Left | Right | Total |
| Bilateral | 0 | 1 | 0 | 1 |
| Left | 3 | 8 | 2 | 13 |
| Right | 1 | 8 | 7 | 16 |
| Total | 4 | 17 | 9 | 30 |

**Table 3. Association between Dominant ear and Site of tumor**

for parotid tumor among people in the age group of 30–39 years of age. Once adjusted for the effect of age, the overall OR came down from the crude OR of 3.47 to 2.86, still retaining its statistical significance (95% CI: 1.03 to 7.97).

## Effect of gender on the association of the exposure and parotid tumor

Though the proportion of men and women were not similar among patients and their controls, stratified analysis suggested that the risk of parotid tumor in those who use mobile phone daily for more than 1 hour was similar among males and females, the ORs being 3.02 (95% CI: 0.85–10.74) and 2.79 (95% CI:0.53–14.67). As the 95% CIs included the null value of 1, the observed ORs were not statistically significant. Once adjusted for the gender differences, the overall OR came down from the crude OR of 3.47 to 2.93, still retaining its statistical significance (95% CI: 1.07 to 8.03)

## Effect of mobile phone brand on the association of the exposure and parotid tumor

None of the patients used Blackberry brand of mobile phone. With proportion of exposure among iPhone users being 9 out of 12 among patients and 4 out of 19 among controls, the odds of exposure was 11.25 (95% CI: 2.04–62.20) times higher among patients compared to controls and the same was statistically significant. The evidence available from 25 Nokia phone users and 16 Samsung users do not seems to suggest that their use for more than 1 hour daily was associated with parotid tumor with ORs being 1.59 (95% CI: 0.24–10.57) among Nokia users and 1.17 (95% CI :0.13–10.22) among Samsung users. The observed effect could as well be due to the artifact of sample size. OR of 3.62 (95% CI: 1.22–10.69), adjusted for the differences in mobile phone brand (without considering Blackberry users) was slightly higher than the crude OR of 3.47.

## Effect of dominant ear used while attending mobile phone on the association of the exposure and parotid tumor

Information on site of the tumor and dominant ear of mobile phone use was available for 30 patients. The site of the tumor was on the right side for 16 (53.3%) patients and left side for 13 (43.3%). One patient had bilateral tumor. Proportion of those who used left, right and both ear dominantly while attending mobile phone was 56.7%, 30% and 13.3%, respectively.

Since number of patients with bilateral tumor and those who used both ears while attending phones were very small, they were excluded for finding out the association between site of tumor and dominant ear of mobile phone use. Table 3

While concordance for the site of tumor and ear of mobile phone use was 80% (8/10) for left sided tumor, it was 46.7% (7/15) for right sided tumor. Fisher's Exact test (the sample size was too small to make the chi–square test valid, hence Fisher's Exact test was preferred) suggested that the association between site of tumor and dominant ear of mobile phone use was not statistically significant ($P = 0.229$). The kappa measure of agreement between the site of tumor and the ear of mobile phone use was 0.24. The measure also was not large enough to be statistically significant ($P = 0.174$).

## Effect of years of mobile phone use on the association of the exposure and parotid tumor

The number of years of mobile phone use does not appear to be a risk factor for the development of parotid tumor in this study. The proportion of exposure among those who were using mobile phones for less than 10 years was 9/14 in patients and 11/33 in controls. It was 9/12 in patients and

13/28 in controls who were using mobile phones for more than 10 years. Among those who used mobile phone for less than 10 years and 10 or more years, the OR was very similar; 3.6 (95% CI: 0.97–13.36) v/s 3.46 (95% CI: 0.77–15.56) and hence adjustment for the differences in the total duration of mobile phone usage did not alter the OR much (OR = 3.54; 95% CI:1.32–9.51) from the crude OR of 3.47.

## Discussion

The results and analysis of the present study suggests an association between the exposure of mobile phone more than 10 hours daily and parotid gland tumor,although no association could be established between the long term use (more than 10 years) of mobile phone and parotid gland tumor. This study also compared the frequency of the dominant ear used and the side of parotid gland affected, the association was not statistically significant.

With the rapid development of the ever–changing field of technology, use of the mobile phones has raised the concern about the radiation these devices emit and their hazardous health consequences [1–4]. The absorption of radiofrequency energy emitted by cellular phones is attenuated by more than 90 percent within 40–50 mm from the exposure source 9. The anatomic location of the parotid gland (at the anterior border of the external ear and between the mandibular ramus and the sternocleidomastoid muscle, 4–10 mm deep in the skin surface) makes it highly susceptible to the radiation exposure and possible subsequent tumor development.

Several studies have suggested the possible health effects involved in the use of hand held mobile phones and their correlations with parotid gland tumors; the finding of this study is in consistent with in a nationwide case control study conducted by Sadetzk et al[6], the association between cellular phone use and development of parotid gland tumors has been shown to be positive. Another 2011 study identified positive association between long term and heavy use of cellular phone and parotid gland malignancy.[10]

In Hardell et al, Auvinen et al, Lonn et al and Söderqvist et al studies[7, 11,12,13], however, no correlation has been discovered between the use of cellular phones and salivary gland tumors. But these studies lacked long term data.

Goldwein et al[8] have studied the influence of handheld mobile phones on human parotid gland secretion. In comparison to the parotid salivary secretion rate and protein concentration between dominant and less dominant sides of subjects from a healthy population who use handheld mobile phones, a significantly higher saliva secretion rate was noticed in the dominant handheld mobile side. Also the total protein concentration was lower in the saliva of the dominant side.

Although the data presented in this study support the hypothesis of association between the exposure to daily mobile phone use of more than 1 hour and parotid tumor, the finding should be interpreted with caution because of relatively small sample size of 26 cases and 61 controls. The observed effect might be an artifact of sample size. The consistency of the finding should be assessed from well–designed case–control studies with larger sample size. The adjustment of OR estimating the association between exposure and parotid tumor, for the effects of factors considered in the study like age, gender, brand of mobile phone, and ear used was carried out by taking only one factor at a time using unconditional logistic regression. Taking all the factors would have given the relative contribution of each of these factors but it was not possible due to relatively small sample size.

There appears to be a general association between the exposure to daily mobile phone use of more than 1 hour and parotid tumor. Further studies with larger sample size need to be conducted for validation and formulating regulations accordingly.

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