LOSS OF SENSE OF SMELL AND TASTE AMONG REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION POSITIVE COVID-19 PATIENTS OF A TERTIARY CARE HOSPITAL: A DESCRIPTIVE CROSS-SECTIONAL STUDY

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ABSTRACT
Introduction
Coronavirus disease (COVID-19) is an ongoing global pandemic that results from infection with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). In patients with COVID-19, anosmia and ageusia can be the first and only symptoms.

Objectives
The aim of the study was to find out the prevalence of Loss of Sense of Smell and Taste among COVID-19 positive patients.

Methodology
This was a descriptive, cross-sectional study of all patients attending department of otorhinolaryngology of Birat Medical College, Nepal February 5 to April 4, 2020. Ethical approval was obtained from the same hospital. Patients with recent onset of loss of smell, taste, or both and patients with other COVID-19 suspected symptoms as per WHO guidelines were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test.

Result
A total of 166 patients were included in the study. The age of the patients ranged from 10 to 84 years with a mean age of 44.34 ±23.059 years. Out of the 166 RT-PCR positive patients 103 (62%) had a loss of taste while 114 (68.7%) had a loss of smell. Nearly half of the subjects about 99 (51.6%) had dysfunction in both taste and smell.

Conclusions
The present study shows the strong association between the olfactory and gustatory dysfunction with that of COVID infection. Patients with loss of taste and smell should be evaluated properly at the time of COVID pandemic. Olfactory and Gustatory dysfunction can be the early and only manifestation of COVID infection. The prevalence of loss of smell and taste was similar to other studies done in similar settings.

KEYWORDS
anosmia; ageusia; COVID-19; reverse transcriptase PCR.
INTRODUCTION

Coronavirus disease (COVID-19) is an ongoing global pandemic that results from infection with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The clinical spectrum of COVID-19 ranges from an asymptomatic or mild flu-like illness to a severe pneumonia and systemic disease requiring critical care. Main symptoms are fever, dry or productive cough, and dyspnea. In patients with COVID-19, anosmia, and ageusia can be the first and only symptoms if the patient is paucisymptomatic. COVID-19 is a highly contagious disease and has human-to-human transmission. COVID-19 was declared a pandemic disease in March 2020 by WHO. Studies have confirmed different degree of loss of smell (anosmia, hyposmia, dysosmia) and loss of taste (dysgeusia, hypogeusia, ageusia) as early symptoms of Covid 19. WHO adopted loss of taste and smell as important discriminatory symptoms of COVID-19. The aim of the study was to find out the prevalence of loss of smell and taste among reverse transcriptase polymerase chain reaction (RT-PCR) positive patients of a tertiary care hospital in Eastern Nepal. Olfactory dysfunction can occur following the upper respiratory tract – called postviral anosmia. However, the precise underlying pathogenesis has not been fully identified when present in COVID-19 cases. Many viruses can cause olfactory dysfunction and ageusia through an inflammatory reaction of the nasal mucosa and causes rhinorrhea. When associated with COVID-19 infections, these alterations seem to have peculiar characteristics, as they are not related to rhinorrhea. Ageusia is the loss of the functions of taste, frequently mistaken for anosmia, since the tongue can only indicate texture and distinguish the tastes perceived through smell.

METHODOLOGY

This was a descriptive cross-sectional study of all patients attending otorhinolaryngology outpatient department of Birat Medical College, Nepal from April 5 to June 4, 2020. This study frame was chosen because the first nationwide lockdown was imposed 24 March 200 when the cases were on the rise and the lockdown was ended on 21 July 2020. Written informed consent was taken for the participation in the study from all the patients. Ethical approval was obtained from institutional review committee of Birat Medical College and Teaching Hospital.

All those patients having complaints of recent onset of loss of smell, taste, or both, and patients with other COVID-19 suspecting features like fever, diarrhea, malaise, etc. as per WHO guidelines were included in the study. Nasopharyngeal and oropharyngeal swab for RT-PCR test for COVID-19 was sent as per government protocol and the result was noted. All those patients fulfilling the inclusion criteria were included in the study and were evaluated. Exclusion criteria for this study was patients not willing to give consent, had trauma, allergic rhinitis, chronic rhinosinusitis, nasal polypsis, psychiatric or neurological disorders, previous surgery or radiation of the nasal or oral cavity, existing smell or taste disturbances.

RESULTS

A total of 166 patients were included in the study. The mean age of the patients was 44.34 ± 23.059 years. The age of the patients ranged from 10 to 84 years. There was a male preponderance 101 patient (60.84%), with female of 65 (39.15%). 62% (103) patients had a loss of taste while 114 (68.7%) had a loss of smell sensation. Fever was seen in 127 (76.5%) of the patients, 86 (51.8%) had a cough, 44 (26.5%) had diarrhea and 42 (25.3%) of subjects had malaise. More than half of the subjects about 98 (59%) had dysfunction in both taste and smell. Those patients who had dysfunction in both smell and test had higher rates of PCR positivity suggesting the study to be statistically significant (p-value < 0.001). Demographic characteristics and symptoms profile amongst the studied population was studied (Table 1).

Table 1. Demographic characteristics and symptoms profile (n=166).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>101 (60.84)</td>
</tr>
<tr>
<td>Female</td>
<td>65 (39.15)</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Loss of Taste</td>
<td>103 (62%)</td>
</tr>
<tr>
<td>Loss of Smell</td>
<td>114 (68.7%)</td>
</tr>
<tr>
<td>Loss of taste and smell (both)</td>
<td>98 (59%)</td>
</tr>
<tr>
<td>Malaise</td>
<td>42 (25.3%)</td>
</tr>
<tr>
<td>Cough</td>
<td>86 (51.8%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>44 (26.5%)</td>
</tr>
<tr>
<td>Fever</td>
<td>127 (76.5%)</td>
</tr>
</tbody>
</table>

This included patients with loss of smell (N=114) and loss of taste (N=103).

Table 2. Gender wise categorization of symptom of loss of taste and smell in RT-PCR positive cases (n=166).

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of Taste</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>68</td>
</tr>
<tr>
<td>Female</td>
<td>35</td>
</tr>
<tr>
<td>Loss of Smell</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74</td>
</tr>
<tr>
<td>Female</td>
<td>40</td>
</tr>
<tr>
<td>Loss of Smell and Taste (both)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>65</td>
</tr>
<tr>
<td>Female</td>
<td>33</td>
</tr>
</tbody>
</table>

This included patients with loss of smell (N=114) and loss of taste (N=103).
DISCUSSION
The first cases of the COVID-19 outbreak started in December 2019 in Wuhan (China) in patients with complicated pneumonia. COVID-19 is a highly contagious disease and has human-to-human transmission. COVID-19 was declared a pandemic disease in March 2020 by WHO. According to The American Academy of Otolaryngology-Head and Neck Surgery (AAHNS) and by the British Rhinology Society (BRS), anosmia, ageusia, and dysgeusia have been reported as symptoms of COVID-19 disease. These two symptoms are also some of the earliest and indicators of COVID-19 and may better predict positivity compared with other symptoms such as fever and cough. Viral infections (common cold, acute rhinosinusitis) of the upper airway can cause olfactory dysfunction. However, the frequency of sensory disorder (taste and/or smell) in the patient affected with COVID-19 is much higher. Patients with COVID-19 gene rally present with symptoms of general malaise, fever, cough, and shortness of breath along with muscle and joint pain, sore throat, headache, nausea, vomiting, diarrhea, and some nasal symptoms (smell and taste dysfunction). Similar to other upper airway viral infections (URTI), such as common cold or flu, the loss of smell is a frequent symptom COVID-19 patients. However, a sudden, severe, and isolated loss of smell and/or taste may also be present in COVID-19 patients who are otherwise asymptomatic.

Many theories have been postulated on the loss of smell and taste in patients with COVID-19. COVID-19 infections use the same receptor [cellular angiotensin-convertingenzyme 2 (ACE2)] as SARS-CoV. This enzyme is found in the tongue. COVID-19 causes taste dysfunction in the same way as ACE2 inhibitors. Among all the symptoms related to COVID-19, both losses of taste and smell were present in more than 50% of the patients in our study. Our study is supported by Agyeman AA in which 47%(up to 80%) of the patients who test positive for COVID19 had a subjective loss of smell and taste. COVID-19 and SARS-COV uses same receptors (Cellular ACE2) and causing degradation of enzymes related to smell and taste sensation. However, the exact mechanism is not yet proven.

Of the many theories 3 major theories has been put forward and is explained in a following way for the loss of smell. First, viral infection triggers inflammation of both respiratory and olfactory mucosa and create a barrier between the dendritic cells of the olfactory sensory neurons and olfactory mucosa, thereby leading to disruption in odor detection. The other mechanism for the loss of smell is by viral infection on the olfactory receptors, which causes the damage with resultant inhibition of transmission of odor signals. The last accepted mechanism explains that the virus is neurotropic and can penetrate through the cribriform plate and can infect the olfactory bulb. It then infects the olfactory cortex of the temporal lobe which is responsible for smell. The coronavirus footprint has been found in the cerebrospinal fluid and brain of COVID-19 patients, thereby clinically verifying viral encephalitis.

Similar study was conducted in Italy in which 60.42% (113/187) of the patients with COVID-19 had an alteration in taste and smell. Full recovery was seen in 55 patients, 46 patients had improvement and no change was seen in 12 patients. A study conducted in Saudi Arabia also found out 64.59% (177/274) of the patients had a loss of smell. Many studies have shown that recent loss of taste and smell is a good predictor for early diagnosis of COVID-19. Loss of taste and smell tend to recover with time in patients suffering from COVID-19. This recovery is because of some transient inflammatory response over the nasal or oral epithelium and the sensory receptors by the virus. A retrospective study was conducted those patients with normal smell function appeared to have a worse course of the disease and were more likely to be hospitalized and placed on a ventilator. This suggests that the patients with smell dysfunction have a milder form of the disease.

This study was conducted in a limited number of patients in three months duration. This study would have been more effective if would have been done in large population and at multiple centers. However, this study will help in knowing the association of olfactory and gustatory dysfunction and provide some data for further studies.

CONCLUSIONS
Our study shows a strong association between the loss of smell and taste with that of COVID-19 infection. Olfactory and gustatory disturbances can be the early presentations of COVID-19. So, in country like Nepal with limited resources of number of beds, medical staff, lack of oxygen, RT-PCR machine, etc. it is better to self-isolate when one suffers from olfactory and gustatory dysfunction as this can be the earliest symptoms. The prevalence of loss of smell and taste was similar to other studies done in similar settings.

RECOMMENDATIONS
This study was conducted in a limited number of patients in three months duration. This study would have been more effective if would have been done in large population and at multiple centers. However, this study will help in knowing the association of olfactory and gustatory dysfunction and provide some data for further studies.
LIMITATIONS OF THE STUDY
The research was conducted in a small group of patients and over a short period of time. RCT and Multicentric study has to be conducted over a longer period of time and larger population to know the exact prevalence of Loss of Sense of Smell and Taste among COVID-19 positive patients.

ACKNOWLEDGEMENT
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CONFLICT OF INTEREST
None

FINANCIAL DISCLOSURE
No financial support was received from anywhere to conduct this study.

REFERENCES