e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(6); 2121-2130

Original Research Article

Smell and Taste Loss in COVID-19: A Mysterious Trait Evading Acquaintance

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Received: 20-03-2023 / Revised: 11-04-2023 / Accepted: 05-05-2023
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Conflict of interest: Nil

Abstract:

Introduction: Severe Acute Respiratory Syndrome Corona virus-2 (SARS CoV-2), emerged as a global pandemic in the late 2019. Its clinical presentation continues to vary with its genetic architecture. Though the ENT symptoms were commonly observed worldwide, its intensity varied among different ethnicity. We intended to survey these symptoms in our state with a special emphasis on Smell and taste loss.

Materials & Methods: This prospective cross-sectional study was done in the state of Puducherry, south India, involving all laboratory confirmed COVID-19 patients who were asymptomatic or mildly symptomatic.

Results: A total of 421 participants were recruited for the study. The mean age was 41 $\pm$ 15 years and 57% were males. 46.3% were aged between 31 to 50 years. Pharyngeal symptoms were the most common 56%, followed by fever 50%. Dysguesia was the most predominant pharyngeal symptom (41%), followed by dry cough (31%). Dysosmia was observed in 35%, which was bilateral in 32%. However, there was no statistical significance observed. Dysguesia and dysosmia recovered within 2 weeks in 54% and 59% respectively. Myalgia, fever, breathlessness, cough with expectoration and hemoptysis were significantly more among the middle aged and the elderly population.

Conclusion: Loss of Smell and altered taste being the most common presentation, it could be used as screening symptom for COVID-19 infection, a guide to implement control measures early, and can serve as an insight into the salient ENT manifestations and its possible sequel.

Keywords: COVID-19, dysosmia, dysguesia, smell and taste loss.

Introduction

Severe Acute Respiratory Syndrome Corona virus-2 (SARS CoV-2), a β corona virus emerged as a global pandemic after being first reported from Wuhan, China in

the late 2019[1,2], causing the Corona Virus Disease -19 (COVID-19). It wreaked havoc across the globe creating panic and took numerous human lives, owing to its high human to human transmissibility [3]. Through the clinical presentation of SARS CoV-2 were identified over time, and it continues to vary with the changes in its genetic architecture. It ranges from mild symptoms like fever, malaise and non-productive cough to severe respiratory distress and multi-organ failure as described in the literature [1,2]. Most of the infected developed mild to moderate symptoms, which were often associated with ear, nose and throat (ENT) symptoms like dysosmia, dysguesia and sore throat.

The ENT symptoms were so commonly observed that, the World Health Organisation (WHO) followed by otologic and rhinologic societies pointed that Smell and Taste Loss (STL) could be used as a potential screening tool for COVID-19[3-11]. Thus, helping in early detection, testing and quarantine. We planned to conduct a survey of these symptoms, especially concerning STL pertaining to the pandemic. We aimed to study the association of ENT symptoms to SARS CoV-2 infection with special emphasis on STL.

Materials and Methods

Our objective was to determine the prevalence of ENT symptoms especially STL and its severity in laboratory confirmed COVID-19 patients, and to determine the time taken towards its recovery. This prospective, cross sectional study was done on laboratory confirmed COVID-19 patients who were asymptomatic or mildly symptomatic, and were treated at a tertiary care teaching hospital in Puducherry, India. Convenience sampling was done. All patients above 10 years of age, confirmed with COVID-19 infection by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), who were asymptomatic or mildly symptomatic were included in this study. Patients who were below 10 years of age, RT- PCR negative, those with prior olfactory or gustatory dysfunction, those who had undergone nasal, sinus or brain surgeries in the past, head injury in the recent past and those who suffered with moderate to severe symptoms requiring oxygen therapy and ICU monitoring were excluded from the study.

Sakali et al [12], reported that the prevalence of dysosmia was 51.2%. Considering an alpha error of 5% and error of margin as 5%, the minimum sample size calculated was 384, using the formula [$n \geq z^2_{1-\alpha/2}pq/d^2$] Where n is the sample size, Z is the statistic corresponding to level of confidence, P is expected prevalence, and d is precision. The final sample size to be achieved was 420 after adding a 10% nonresponse rate.

All these patients were administered a questionnaire pertaining to their presenting symptoms, ENT manifestations and STL. A pre-validated modified questionnaire, adopted from AAOHNS (American Association of Otolaryngology and Head & Neck Surgery) tool for diagnosing anosmia was used to suit our patients. They were also asked to quantify their smell and taste disturbances on a scale of 1 to 10 in comparison to pre COVID status. The questionnaire was administered personally to the patients admitted in the hospital, and also through telephonic conversation or Google forms. All the patients were followed up for 4 to 6 weeks from the date of declaration of throat swab results, to ascertain the time taken for the recovery of STL, through telephonic conversation.

The data was stored in MS Excel and analysed using SPSS version 20. Categorical data were represented using frequency and percentage. Quantitative data were represented using mean and standard deviation. To find the association between variables, Chi square test was

used for qualitative data and Student's t test was used for quantitative data.

P- Value (< 0.05) was considered significant.

Results: A total of 421 participants were recruited for the study, the mean age was 41 ± 15 years (range 12 to 85 years). Among the total 421 patients 239 (57%) were male. The participants were divided into three groups based on their age distribution, 115 (27.3%) were aged less than 30 years, 195 (46.3%) were aged between 31 to 50 years and the rest 111 (26.4%) were older than 50 years (Table 1).

Table 1: Demographic details of the study population

Variable	N	Minimum	Maximum	Mean	Std. Deviation
Age	421	12	85	41.10	15.142
		Frequency	Percent	Valid Percent	Cumulative Percent
Sex	Female	182	43.2	43.2	43.2
	Male	239	56.8	56.8	100.0
Age category	<30 years	115	27.3	27.3	27.3
	31-50 years	195	46.3	46.3	73.6
	>50 years	111	26.4	26.4	100.0
Throat swab	Positive	421	100.0	100.0	100.0

The preliminary assessment of symptoms revealed that, the pharyngeal symptoms were the most common 237 (56%), followed by fever in 211 (50%). Other less common symptoms included those pertaining to nose 171 (40%), and headache in 121 (29%) participants. Aural symptoms were the least observed 37 (9%), only next to breathlessness 54(30%) and cough with expectoration 70(6%) (Table 2).

Table 2: General distribution of symptoms pertaining to Ear, Nose and Throat

Variables	Sub group	Age Group (in Years)			P Value	Gender group		P Value
		Less than 30 (N=115)	31 – 50 (N=195)	more than 50 (N=111)		Male (N=239)	Female (N=182)	
Ear	Yes	8 (6.96%)	19 (9.74%)	10 (9.01%)	0.701	16 (6.69%)	21 (11.53%)	0.082
	No	107 (93.04%)	176 (90.26%)	101 (90.99%)		223 (93.31%)	161 (88.46%)	
Nose	Yes	42 (36.52%)	91 (46.67%)	38 (34.23%)	0.06	89 (37.23%)	82 (45.05%)	0.106
	No	73 (63.48%)	104 (53.33%)	73 (65.77%)		150 (62.76%)	100 (54.94%)	
Throat	Yes	54 (46.96%)	118 (60.51%)	65 (58.56%)	0.057	131 (54.8%)	106 (58.2%)	0.482
	No	61 (53.04%)	77 (39.49%)	46 (41.44%)		108 (45.2%)	76 (41.8%)	

Among the pharyngeal symptoms, the loss of taste or altered taste was the most predominant 171 (41%), followed by dry cough 131 (31%), sore throat 94 (22%), and dysphagia 31 (7%) (Table 3).Among the nasal symptoms, anosmia or altered smell was the most commonly observed, in 149 (35%) participants, followed by nasal block in 98(23%), nasal discharge in 88(21%) and epistaxis in one participant. The smell sense was altered bilaterally in 135 (32%) and only on the right sided in 14(3%) participants (Table 3). The aural symptoms were the least observed. Vertigo was the most predominant 20(5%), followed by ear block 16(4%), and hearing

loss 18(4%). Other less common symptoms observed were, sneezing 24(6%), postnasal drip 11(3%), facial pain 21(5%) and hemoptysis 6(1%) (Table 3).

Table 3: Association of other Symptoms in relation to age group and gender

Variables	Sub group	Age Group (in Years)			P Value	Gender group		P Value
		Less than 30 (N=115)	31 – 50 (N=195)	more than 50 (N=111)		Male (N=239)	Female (N=182)	
Pain In Right Ear	Yes	0 (0%)	1 (0.51%)	1 (0.9%)	0.612	1 (0.4%)	1 (0.5%)	0.846
	No	115 (100%)	194 (99.5%)	110 (99.1%)		238(99.6%)	181 (99.5%)	
Pain In Left Ear	Yes	0	1 (0.5%)	1 (0.9%)	0.612	1 (0.4%)	1 (0.5%)	0.846
	No	115 (100%)	194 (99.5%)	110 (99.1%)		238 (99.6%)	181 (99.5%)	
Ear Block Right Side	Yes	2 (1.74%)	6 (3.08%)	2 (1.8%)	0.68	5 (2.1%)	5 (2.7%)	0.66
	No	113 (98.3%)	189 (96.9%)	109 (98.2%)		234 (97.9%)	177 (97.3%)	
Ear Block Left Side	Yes	2 (1.7%)	4 (2.1%)	0	0.328	4 (1.7%)	2 (1.1%)	0.622
	No	113 (98.3%)	191 (97.9%)	111 (100%)		235 (98.3%)	180 (98.9%)	
Hearing Loss Right Side	Yes	2 (1.7%)	1 (0.5%)	5 (4.5%)	0.048	4 (1.7%)	4 (2.2%)	0.7
	No	113 (98.3%)	194 (99.5%)	106 (95.5%)		235 (98.3%)	178 (97.8%)	
Hearing Loss Left Side	Yes	1 (0.9%)	1 (0.5%)	6 (5.4%)	0.007	3 (1.3%)	5 (2.7%)	0.26
	No	114 (99.1%)	194 (99.5%)	105 (94.6%)		236 (98.7%)	177 (97.3%)	
Vertigo /Giddiness	Yes	6 (5.2%)	12 (6.1%)	2 (1.8%)	0.219	8 (3.3%)	12 (6.6%)	0.121
	No	109 (94.8%)	183 (93.8%)	109 (98.2%)		231 (96.7%)	170 (93.4%)	
Sneezing	Yes	9 (7.8%)	13 (6.67%)	2 (1.8%)	0.108	11 (4.6%)	13 (7.1%)	0.265
	No	106 (92.2%)	182 (93.3%)	109 (98.2%)		228 (95.4%)	169 (92.9%)	
Right Nasal Block	Yes	10 (8.7%)	37 (18.9%)	9 (8.11%)	0.006	30 (12.6%)	26 (14.3%)	0.604
	No	105 (91.3%)	158 (81.0%)	102 (91.9%)		209 (87.4%)	156 (85.7%)	
Left Nasal Block	Yes	8 (6.9%)	36 (18.5%)	9 (8.1%)	0.003	29 (12.1%)	24 (13.2%)	0.747
	No	107 (93.0%)	159 (81.5%)	102 (91.9%)		210 (87.9%)	158 (86.8%)	
Right Nasal Discharge	Yes	11 (9.6%)	25 (12.8%)	9 (8.1%)	0.396	24 (10%)	21 (11.5%)	0.622
	No	104 (90.4%)	170 (87.2%)	102 (91.9%)		215 (90%)	161 (88.5%)	
Left Nasal Discharge	Yes	13 (11.3%)	23 (11.8%)	7 (6.3%)	0.282	21 (8.8%)	22 (12.1%)	0.268
	No	102 (88.7%)	172 (88.2%)	104 (93.7%)		218 (91.2%)	160 (87.9%)	
Right Nasal Bleeding	Yes	1 (0.87%)	0 (0%)	0 (0%)	0.264	0	1 (0.5%)	0.251
	No	114 (99.1%)	195 (100%)	111 (100%)		239 (100%)	181 (99.5%)	
Post Nasal	Yes	4 (3.48%)	7 (3.59%)	0 (0%)	0.132	5 (2.1%)	6 (3.3%)	0.44

Drip	No	111 (96.5%)	188 (96.4%)	111 (100%)		234 (97.9%)	176 (96.7%)	3
Sore Throat	Yes	22 (19.13%)	48 (24.62%)	24 (21.62%)	0.523	50 (20.9%)	44 (24.2%)	0.427
	No	93 (80.9%)	147 (75.4%)	87 (78.4%)		189 (79.1%)	138 (75.8%)	
Difficulty In Swallowing	Yes	10 (8.7%)	15 (7.7%)	6 (5.4%)	0.621	21 (8.8%)	10 (5.5%)	0.2
	No	105 (91.3%)	180 (92.3%)	105 (94.6%)		218 (91.2%)	172 (94.5%)	
Dry Cough	Yes	23 (20%)	67 (34.4%)	41 (36.9%)	0.009	84 (35.1%)	47 (25.8%)	0.041
	No	92 (80%)	128 (65.6%)	70 (63.1%)		155 (64.9%)	135 (74.2%)	
Head Ache	Yes	28 (24.3%)	64 (32.8%)	29 (26.1%)	0.219	58 (24.3%)	63 (34.6%)	0.02
	No	87 (75.6%)	131 (67.2%)	82 (73.9%)		181 (75.7%)	119 (65.4%)	
Facial Pain	Right Side	1 (0.9%)	3 (1.5%)	1 (0.9%)	0.327	3 (1.3%)	2 (1.1%)	0.848
	Bilateral	7 (6.09%)	8 (4.1%)	1 (0.9%)		8 (3.3%)	8 (4.4%)	
	No	107 (93%)	184 (94.4%)	109 (98.2%)		228 (95.4%)	172 (94.5%)	
Generalized Myalgia	Yes	35 (30.4%)	105 (53.8%)	60 (54.1%)	<0.01	112 (46.9%)	88 (48.4%)	0.762
	No	80 (69.6%)	90 (46.2%)	51 (45.9%)		127 (53.1%)	94 (51.6%)	
Fever	Yes	41 (35.7%)	107 (54.9%)	63 (56.8%)	<0.01	116 (48.5%)	95 (52.2%)	0.457
	No	74 (64.3%)	88 (45.1%)	48 (43.2%)		123 (51.5%)	87 (47.8%)	
Breathlessness	Yes	4 (3.5%)	29 (14.9%)	21 (18.9%)	<0.01	25 (10.5%)	29 (15.9%)	0.096
	No	111 (96.5%)	166 (85.1%)	90 (81.1%)		214 (89.5%)	153 (84.1%)	
Cough With Expectoration	Yes	9 (7.8%)	38 (19.5%)	23 (20.7%)	0.012	40 (16.7%)	30 (16.5%)	0.945
	No	106 (92.2%)	157 (80.5%)	88 (79.3%)		199 (83.3%)	152 (83.5%)	
Hemoptysis	Yes	1 (0.9%)	3 (1.5%)	2 (1.8%)	0.826	5 (2.1%)	1 (0.5%)	0.186
	No	114 (99.1%)	192 (98.5%)	109 (98.2%)		234 (97.9%)	181 (99.5%)	

The time taken for the recovery of altered taste or dysguesia varied, it was 2 weeks in 93 (54%), 3 weeks in 32 (19%), 4 weeks in 28 (16%) and took more than 4 weeks in 7 (<1%) patients. The recovery time for anosmia or altered smell was similar to that observed with dysguesia. The recovery time was 2 weeks in 88(59%), 3 weeks in 22 (15%), 4 weeks in 19(13%), and more than 4 weeks in 9(<1%) (Table 4).

Table 4: Comparison of smell and taste disturbances among various age groups and gender

Variables	Sub group	Age Group (in Years)			P Value	Gender group		P Value
		Less than 30 (N=115)	31 – 50 (N=195)	more than 50 (N=111)		Male (N=239)	Female (N=182)	
Loss Of Smell	Yes	38 (33.0%)	84 (43.1%)	37 (33.3%)	0.113	85 (35.6%)	74 (40.7%)	0.285
	No	77 (67.0%)	111 (56.9%)	74 (66.7%)		154 (64.4%)	108 (59.3%)	
Loss of Taste	Yes	38 (33.0%)	90 (46.2%)	43 (38.7%)	0.068	90 (37.7%)	81 (44.5%)	0.156
	No	77 (67.0%)	105 (53.8%)	68 (61.3%)		149 (62.3%)	101 (55.5%)	
Time Taken for Recovery of Taste Sense	2 Weeks	28 (24.3%)	55 (28.2%)	17 (15.3%)	0.018	55 (23.0%)	45 (24.7%)	0.427
	3 Weeks	7 (6.1%)	20 (10.3%)	13 (11.7%)		18 (7.5%)	22 (12.1%)	
	4 Weeks	5 (4.3%)	10 (5.1%)	14 (12.6%)		17 (7.1%)	12 (6.6%)	
	>4 Weeks	1 (0.9%)	6 (3.1%)	1 (0.9%)		6 (2.5%)	2 (1.1%)	
	NIL	74 (64.3%)	104 (53.3%)	66 (59.5%)		143 (59.8%)	101 (55.5%)	
Time Taken for Recovery of Smell Sense	2 Weeks	25 (21.7%)	56 (28.7%)	13 (11.7%)	0.001	52 (21.8%)	42 (23.1%)	0.144
	3 Weeks	5 (4.3%)	12 (6.2%)	12 (10.8%)		10 (4.2%)	19 (10.4%)	
	4 Weeks	3 (2.6%)	7 (3.6%)	11 (9.9%)		13 (5.4%)	8 (4.4%)	
	>4 Weeks	2 (1.7%)	8 (4.1%)	0 (0%)		6 (2.5%)	4 (2.2%)	
	NIL	80 (69.6%)	112 (57.4%)	75(67.6%)		158 (66.1%)	109 (59.9%)	

We did not find any significant association of presenting symptoms with respect to gender except for headache and dry cough, which were more common among the women. But we noticed significant difference among the various age groups. The presenting symptoms such as, myalgia, fever, breathlessness, cough with expectoration and hemoptysis were significantly more among the middle aged and the elderly population. With respect to smell and taste loss, we were surprised to note that we did not observe any significant loss of smell with respect to age groups (p=0.1) or gender (p=0.2) (Table 4), which was reinforced by the significant absence of nasal block (right side p=0.006, left side p=0.003) (Table 3). Neither did we observe any significant loss of taste among the age groups (p=0.06) or gender (p=0.15) (Table 4). The findings were consistent with the significant absence of hearing loss as well (right ear p=0.04, left ear p=0.007) (Table 3).

Discussion

The world faced a novel coronavirus named the COVID-19, which emerged as a pandemic and took away numerous lives daily. The lack of specific treatment or effective vaccine in the early phases of the outbreak made the situation even worse. The only way to prevent its spread was by early detection and strict isolation. Which

was achieved by studying the symptomatology of this viral infection. Numerous studies were published in the early phases of the pandemic emphasizing the symptomatology of this viral infection. But COVID-19 surprised everyone with the varying symptoms among different regions and ethnicity, although with some overlap. Sore throat, nasal congestion, rhinorrhea, fatigue, breathlessness, conjunctivitis, headache and fever were some of the most commonly observed symptoms along with the most peculiar symptom of Smell and Taste Loss (STL)[13].

Upper respiratory tract infections are known to cause temporary alteration in smell and taste through inflammation of the nasal mucosa and rhinorrhoea. The common viral pathogens associated are Rhinovirus, Parainfluenza, Epstein-Barr virus and Coronavirus. However, absence of rhinorrhea with STL was a peculiar feature observed with COVID-19 infection [5, 6].

In our study, out of the total 421 paricipants, 65% were normosmic and only 35% had hyposmia. This was in contrast to Jan C Luers et al [14] and Lechien et al [1], who observed olfactory dysfunction in 70% and 85.6% of patients respectively. A review of 5 articles on COVID-19 from china done by Lovato and De Filippis [15] did not report any olfactory dysfunction, also the study by Mao et al [16] in Wuhan China observed impaired smell in only 5% of patients. Thus, what we perceived from the above studies was that, the prevalence of olfactory dysfunction is not uniform and it varied in different races. Seiden et al [17] observed that the prevalence of olfactory dysfunction in upper respiratory tract infection is around 22% to 36%, and a similar prevalence was noticed in our study as well. Most of the patients who experienced hyposmia were in the age group of 31-50 years followed by those less than 30 years of age. Overall, the hyposmia / altered smell observed was more common among the middle age (41%) and younger age group (32%), and predominantly among men (80%). These findings were similar to those reported by Manoj et el [18] who observed olfactory dysfunction in 36% of patients. Among the other Indian studies, Khare et al[19] reported that the smell disturbance was 49% for a single odorant and 22 % for two odorants and Mishra et al [20] reported its prevalence be 15 %, which were consistent with our observations.

The exact mechanism of such dysfunction is not known. Corona virus are known to be neuroinvasive or neurotropic, animal experiments on mice demonstrated that the virus entered brain through olfactory bulb [21]. The key genes responsible for such entry are the ACE-2(angiotensin converting enzyme) and TMPRSS2. The expression of ACE-2 is highest among the nasal epithelial cells, which explains why nasal epithelium is targeted by viruses [22].

However, the olfactory bulb do not express ACE-2 and TMPRSS2 and thus, failed to explain this hypothesis. Brann et al [23] reported that the olfactory epithelial supporting cells, sustentacular cells, stem cells and perivascular cells express ACE-2. Hence, it is hypothesized that the olfactory involvement of SARS CoV-2 may be due to non-neural cell impairment instead of olfactory sensory neuron involvement. The inflammatory process involving the non-neural structures could lead to diffuse architectural damage and may interfere with the signaling of olfactory sensory neurons [24].

On the other hand, Dysguesia may occur secondary to smell dysfunction or due to direct injury by viral infection. Xu et al [25], reported high expression of ACE-2 receptor on the epithelial cells of oral mucosa and tongue, which confirms the hypothesis of direct injury.

In our study, the maximum recovery of hyposmia occurred within 2 weeks of its commencement. The recovery rate was faster and higher among the middle and younger age groups. Although we expected higher prevalence and delayed recovery of hyposmia among the older age group, the observations made were to the contrary, showing that middle aged patients were affected more. We believe that these observations could have resulted due to non-inclusion of sick patients / patients requiring oxygen therapy, who were largely elderly or middle aged.

There is no specific treatment for COVID-19 induced olfactory loss, although nasal steroids have been offered with some effect. However, the recovery of smell and taste in our study was high, mitigating specific treatment or intervention.

To our knowledge, this is the first study in the state of Puducherry, done to assess the frequency and outcome of STL among COVID-19 patients. A Large sample size and real time PCR confirmed patients offered great strength to our study. However, the results were largely derived from patient's subjective assessment. We could not perform objective assessment in order to reduce the risk of infection transmission substantially.

Limitations:

The COVID-19 situation was a serious health emergency, collection of data and analysis were increasingly difficult.

The lack of precisely defined clinical manifestations and variations in the clinical manifestation from time to time was a major hurdle faced during the study.

ENT endoscopy or radiological screening could not be performed in view of huge number of cases in a short period, limited infrastructure and also the substantial risk of infection transmission.

Conclusion

We conclude that ENT manifestations occur concurrently with COVID 19 infection. Loss of Smell and altered taste being the most common presentation, and thus, could be used as screening symptoms for COVID infection. The COVID-19 infection has been a challenge worldwide, as the virus keeps evolving and so does the manifestations and complications. A better understanding of the virus is necessary to assess its implications on the human kind. We hope that our study will serve as a step towards further research, a guide to implement control measures early, an insight into the salient ENT manifestations and its possible sequel.

Funding

All the authors certify that we did not receive any support or funding from any organization for the submitted work or to assist with the preparation of this manuscript.

Ethics committee approval

The present study was done at Indira Gandhi Medical College & Research Institute (IGMC&RI) Puducherry, from May 2019 to May 2020 after obtaining clearance from the Institute Ethical Committee (Proposal No. 26/207/IEC-25/PP/2019)

Consent to participate

All The authors affirm that Informed consent was obtained from all individual participants included in the study.

Acknowledgements

I would like to thank the ENT PG residents Dr. Abinaya, Dr. Prathiba, and Junior Resident Dr. Buvaneshwari who were of immense help during the data collection, followup and compilation.I would like to sincerely thank all the interns posted at IGMCRI without whom, this study would not have been made possible.I would like to thank all the participants of this study, who came forward to

participate in this study despite their illness and made this study possible.

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