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A Comparative Study to Assess Utility of Olfactory and Gustatory Dysfunctions in the Diagnosis of COVID-19

Dr. Sheshan VS[1], Dr. Amruthavarshini N[2], Dr. Lokesh M[3*], Dr. Vikas N[4], Dr. Naryanaswamy[5]

[1]Senior Resident, Department of Medicine, Dr. B R Ambedkar Medical College Karnataka India
[2-4]Post Graduate Student, Department of Medicine, Bangalore Medical College and Research Institute, Karnataka, India
[5]Professor, Department of Medicine, Bangalore Medical College and Research Institute, Karnataka, India

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***Corresponding author:** Dr. Lokesh M

Abstract **Original Research Article**

Background: COVID-19 is a pandemic that has infected more than 100 million individuals, clinical presentations varies from common cold like symptoms to severe acute respiratory illness; olfactory and gustatory dysfunction may be presenting /concurrent/delayed symptoms in COVID 19 infection. ***Methods*:** In this prospective observational study, 60 COVID- 19 positive patients and 60 COVID negative/suspect patients respectively were enrolled from march 2020 to July 2020 in Bowring and lady Curzon Hospital, Bangalore and they were assessed for taste and smell sensations based on SQOD- NS and questions based on smell and taste component of NHNE survey, symptomatic patients were followed up and duration needed for recovery of symptoms was analysed for P value, chi-square value, other relevant blood and radiological investigations were done. ***Results*:** Among 60 COVID 19 positive patients, males were 43 (35.8%) and females were 17(14.2%) and Among 60 COVID negative/Suspects, males were 39, females were 21.Among COVID 19 positive group 15 patients had Anosmia, 29 patients had Hyposmia, 16 patients had no loss of smell .Recovery time for smell following infections takes >15days for 12 patients, 9-14 days for 26 patients, 4-8 days for 17 patients and, 1-4 days for 5 patients, but most of COVID negative /suspects about 48 patients were taken 1-4 days recovery of smell and the P value was 0.00 and Chi-square value was 68.74 which were statistically significant. ***Conclusion*:** We concluded that patients with COVID 19 positive status had severe spectrum of olfactory dysfunction like anosmia, hyposmia and they will have long recovery time compared to COVID negative /suspect patients. Taste perception was more impaired in COVID positive patients compared to COVID negative /suspects. Covid positive patients had higher sQOD-NS score compared to COVID negative patients and significant associations are seen. Hence these symptoms can aid in diagnosis of COVID-19 which can be further confirmed by confirmatory tests.

Keywords: COVID-19, acute respiratory illness, COVID patients, Diagnosis.

INTRODUCTION

The World Health Organization (WHO) estimates that acute respiratory infections (ARI) cause annual deaths approaching 4 million, at a rate of more than 60 deaths/ 100,000 populations. Viruses are responsible for 30-70 % of ARI where respiratory syncytial virus (RSV), influenza virus, parainfluenza virus (PIV), human Bocavirus, human metapneumovirus (hMPV), adenovirus, rhinovirus, enterovirus and Coronaviruses account for the majority of these cases.

Sudden onset olfactory dysfunction may be the only presenting feature in some patients with COVID-19 infection, especially in the initial stage of the disease. Complete and partial loss of smell known as anosmia and hyposmia respectively, are commonly experienced by patients with COVID 19. However, unlike other viral infections, olfactory dysfunction associated with COVID 19 infection is often not associated with rhinorrhea or nasal obstruction. Although the exact pathogenesis remains elusive, olfactory epithelial damage and central nervous system involvement have been described as the probable cause. High angiotensin converting enzyme 2 (ACE-2) and transmembrane protease serine 2 (TMPRSS-2) expression in nasal epithelial cells allows for a wide viral entry and thus damage to olfactory sensory neurons. Invasion of the olfactory bulb has also been hypothesized as a mechanism of virus- induced anosmia.

The definite diagnosis of COVID-19 mostly relies on positive RT-PCR on respiratory samples, although discriminant features have been reported on

thoracic CT scan [1]. However, access to these diagnostic tests is limited in the context of this large-scale pandemic.

Anosmia/hyposmia is often associated with loss (ageusia) or alteration (dysgeusia) of taste sensation. Loss of smell and taste adversely affects the appetite as well as the mood and may negatively impact the patient's quality of life.

Distinctive clinical features would be welcome to better select patients who require investigations. During the early phase of the COVID-19 outbreak in France, many patients reported loss of smell (hyposmia) and taste (hypogeusia) [2], Taste and smell disorders have been associated with herpes zoster and HIV3,4. The neuroinvasive potential of SARS-CoV-2 might have a role in the pathophysiology of hypogeusia and hyposmia [5]. As the olfactory mucosa is located in the upper region of the nasal cavity, a direct or indirect effect of SARS-CoV-2 in situ might be another explanation for these symptoms. The prevalence of taste and smell disorders in patients with COVID-19 was estimated to be 5% in a previous study [6].

OBJECTIVES OF THE STUDY

1. To compare the olfactory and gustatory dysfunctions in COVID suspects and patients with laboratory-confirmed COVID-19 infection.
2. To assess utility of hypoguesia and hyposmia as discriminant clinical features that might be used for the diagnosis of COVID-19 in patients with ILI.

Inclusion Criteria

1. Age >18 years <60 years of either gender.
2. Patient willing to give written informed consent.
3. Patients with influenza like illness with RT-PCR negative/COVID suspect.
4. Laboratory confirmed COVID -19 positive patients by RT-PCR**.**

Exclusion Criteria

1. Patient not willing to give informed consent.
2. Pre-existing gustatory and olfactory dysfunctions like DNS, nasal polyposis, chronic rhinosinusistis.
3. Patients who are admitted in HDU and ICU.

METHODOLOGY

In this prospective observational study, 60 COVID- 19 positive patients and 60 COVID negative/suspect patients respectively were enrolled from march 2020 to July 2020 in Bowring and lady Curzon Hospital, Bangalore and they were assessed for taste and smell sensations based on SQOD- NS and questions based on smell and taste component of NHNE survey. Patients with laboratory-confirmed COVID-19 infection recruited from BMCRI hospitals. The following epidemiological and clinical outcomes will be studied: age, sex, and comorbidities, general, olfactory and gustatory sensations. COVID 19 suspects and confirmed patients after taking consent will be assessed for taste and smell sensations based on validated short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) by the National Health and Nutrition Examination Survey. If found to have symptoms patient will be followed up and duration needed for recovery of symptoms will be assessed. This is a 7-item patient-reported outcome questionnaire including social, eating, annoyance, and anxiety questions. Each item is rated on a scale of 0-3, with higher scores reflecting better olfactory-specific QoL. The total score ranges from 0 (severe impact on QoL) to 21 (no impact on QoL) . The rest of the olfactory and gustatory questions were based on the smell and taste component of the National Health and Nutrition Examination Survey . The questions have been chosen to characterise the variation, timing and associated-symptoms of both olfactory and gustatory dysfunctions, and, therefore, they suggest a potential aetiology. The mean recovery time of olfaction will be assessed through 4 defined propositions: 1-4 days; 5-8 days; 9-14 days and >15 days.

STATISTICAL METHODS

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.** Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data are made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters.

RESULTS

The present study was conducted in the Department of Medicine, Bangalore Medical College and Research Institute. A total of 120 cases of both COVID-19 positive and COVID negative/suspects were taken and the data obtained thereby are presented and analysed below.

In this study total 60 COVID-19 positive patient and total 60 COVID-19 negative/suspect we're enrolled, Among COVID-19 positive patient, males were 43 and females were 17 and among 60 patients of

COVID negative/Suspect status, males were 39, females were 21.

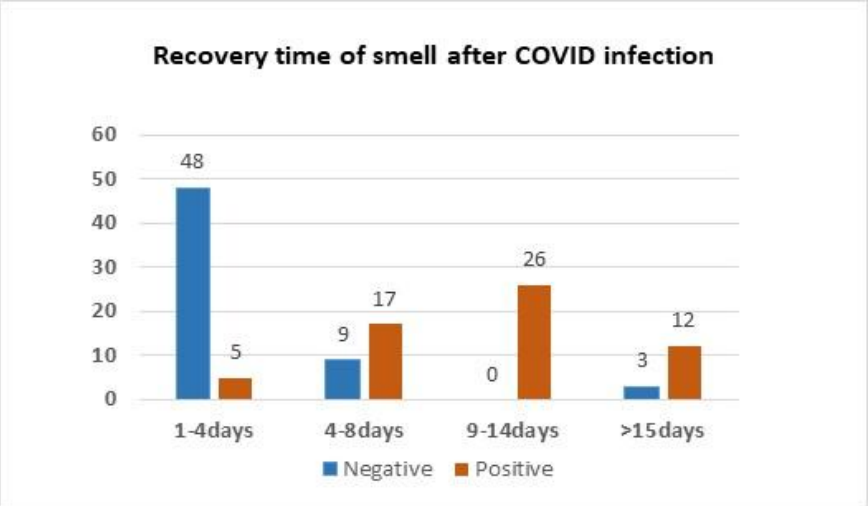

Fig-1: Distribution of the recovery time among the groups

Table-1: Distribution of the recovery time among the groups

Recovery time of smell after COVID infection or during COVID infection		Groups		Total
		Negative	Positive	
>15days	Count	3	12	15
	%	2.5%	10.0%	12.5%
1-4days	Count	48	5	53
	%	40.0%	4.2%	44.2%
4-8days	Count	9	17	26
	%	7.5%	14.2%	21.7%
9-14days	Count	0	26	26
	%	0.0%	21.7%	21.7%
Total	Count	60	60	120
	%	50.0%	50.0%	100.0%
Chi-square value- 68.74				
p value-0.00*				

*significant

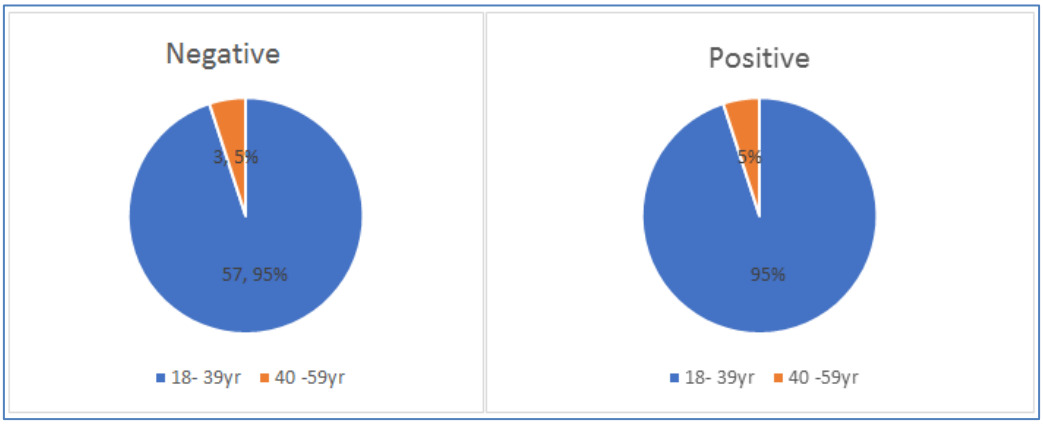

Fig-2: Distribution of the age among the groups

Table- 2: Distribution of the age among the groups

Age		Groups		Total
		Negative	Positive	
18- 39yr	Count	57	57	114
	%	47.5%	47.5%	95.0%
40 -59yr	Count	3	3	6
	%	2.5%	2.5%	5.0%
Total	Count	60	60	120
	%	50.0%	50.0%	100.0%
Chi-square value- 0.00				
p value-1.00				

Patients of both COVID positive and COVID negative groups have same age distribution, as age per se there is no significant association of age with this study, in which p value -1.00 and chi square value -0.00.

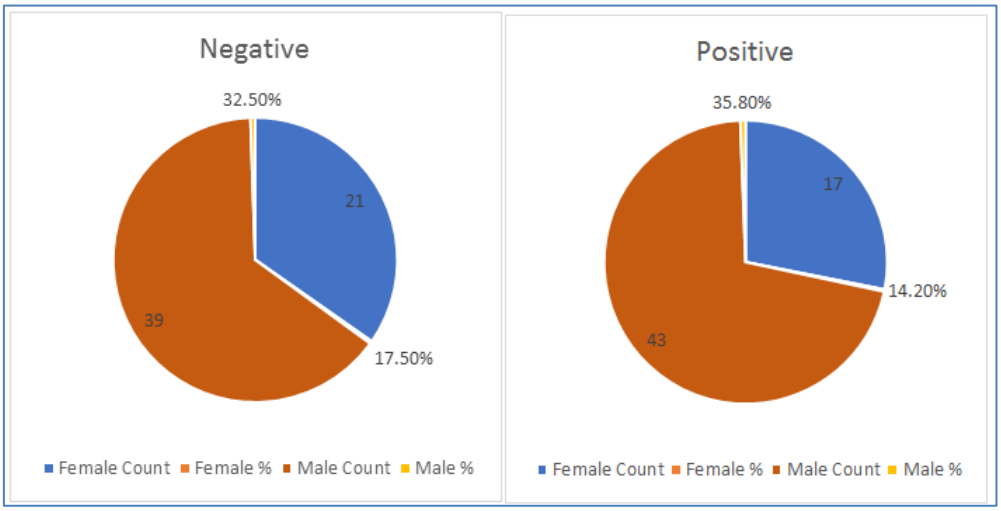

Fig-3: Distribution of the gender among the groups

In this study total 60 COVID-19 positive patients and total 60 COVID-19 negative/suspect were enrolled. Total 38 females and 82 males were enrolled in the study Among COVID-19 positive patient, males were 43 and females were 17 and among 60 patients of COVID negative/Suspect status, males were 39, females were 21. But there is no association between COVID positive and COVID negative group with related to gender in which p value of study is 0.43 and Chi-square value-0.61.

Table-3: Distribution of the gender among the groups

Gender		Groups		Total
		Negative	Positive	
Female	Count	21	17	38
	%	17.5%	14.2%	31.7%
Male	Count	39	43	82
	%	32.5%	35.8%	68.3%
Total	Count	60	60	120
	%	50.0%	50.0%	100.0%
Chi-square value- 0.61				
p value-0.43				

Table-4: Distribution of the responses

Questions	Responses		Groups		Total	Chi-square value	p value
			COVID Negative	COVID Positive			
Past history of Allergy (asthma or Rhinitis	No	Count	39	49	88	4.26	0.039*
		%	32.5%	40.8%	73.3%		
	Yes	Count	21	11	32		
		%	17.5%	9.2%	26.7%		
Past history during Covid infection	Diabetes	Count	1	2	3	3.36	0.33
		%	.8%	1.7%	2.5%		
	Hypertension	Count	1	0	1		
		%	.8%	0.0%	.8%		
	Nil	Count	58	56	114		
		%	48.3%	46.7%	95.0%		
	Others	Count	0	2	2		
		%	0.0%	1.7%	1.7%		
Fever history during covid infection	Nil	Count	60	11	71	82.81	0.00*
		%	50.0%	9.2%	59.2%		
	Yes	Count	0	49	49		
		%	0.0%	40.8%	40.8%		
Running nose during infection	No	Count	33	44	77	4.38	0.036*
		%	27.5%	36.7%	64.2%		
	Yes	Count	27	16	43		
		%	22.5%	13.3%	35.8%		
Nasal obstruction during covid infection	No	Count	33	46	79	6.26	0.012*
		%	27.5%	38.3%	65.8%		
	Yes	Count	27	14	41		
		%	22.5%	11.7%	34.2%		
Sore throat during covid infection	No	Count	24	20	44	0.57	0.44
		%	20.0%	16.7%	36.7%		
	Yes	Count	36	40	76		
		%	30.0%	33.3%	63.3%		
Dyspnea during covid infection	No	Count	36	52	88	10.9	0.001*
		%	30.0%	43.3%	73.3%		
	Yes	Count	24	8	32		
		%	20.0%	6.7%	26.7%		
Loss of taste during covid infection	No	Count	51	23	74	27.63	0.00*
		%	42.5%	19.2%	61.7%		
	Yes	Count	9	37	46		
		%	7.5%	30.8%	38.3%		
Smoking Habits	No	Count	53	53	106	0.00	1.00
		%	44.2%	44.2%	88.3%		
	Yes	Count	7	7	14		
		%	5.8%	5.8%	11.7%		
Degree of losing smell during covid infection	Complete loss of smell (Anosmia)	Count	0	15	15	38.04	0.00*
		%	0.0%	12.5%	12.5%		
	Decreased perception of smell (Hyposmia)	Count	12	29	41		
		%	10.0%	24.2%	34.2%		
	No loss of smell	Count	48	16	64		
		%	40.0%	13.3%	53.3%		
Changes in my sense of smell isolate me socialy	No	Count	54	54	108	1.00	0.00*
		%	45.0%	45.0%	90.0%		
	Yes	Count	6	6	12		
		%	5.0%	5.0%	10.0%		
The problems with the my sense of smell have a negative impact on my daily social activities	No	Count	51	35	86	10.5	0.001*
		%	42.5%	29.2%	71.7%		
	Yes	Count	9	25	34		
		%	7.5%	20.8%	28.3%		
The problems with my sense of smell that make me more irritable	No	Count	51	42	93	3.87	0.049*
		%	42.5%	35.0%	77.5%		
	Yes	Count	9	18	27		
		%	7.5%	15.0%	22.5%		
Because of the problem with my sense of smell, I will eat	No	Count	47	35	82	5.54	0.019*
		%	39.2%	29.2%	68.3%		

out less	Yes	Count	13	25	38		
		%	10.8%	20.8%	31.7%		
Because of the problem with my sense of smell, I will eat less than before(loss of apetite)	No	Count	48	34	82	7.54	0.006*
		%	40.0%	28.3%	68.3%		
	Yes	Count	12	26	38		
		%	10.0%	21.7%	31.7%		
Because of the problem with my sense of smell, I have to make more effort to relax	No	Count	54	44	98	5.56	0.018*
		%	45.0%	36.7%	81.7%		
	Yes	Count	6	16	22		
		%	5.0%	13.3%	18.3%		
I 'm afraid I'll never be able to get used to the problems with my sense of smell.	No	Count	60	48	108	13.33	0.00*
		%	50.0%	40.0%	90.0%		
	Yes	Count	0	12	12		
		%	0.0%	10.0%	10.0%		

*significant

Each questions of a validated short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) by the National Health and Nutrition Examination Survey shows significant associations of olfactory dysfunction in COVID positive patients.

Table-5: Cross tabulation of recovery time of smell and degree of losing smell during covid infection

Groups	Recovery time of smell		Degree of losing smell during Covid infection			Total	Chi-square value	p value
			Anosmia	Hyposmia	No loss of smell			
Negative	>15days	Count	0	0	3	3	1.79	0.4
		%	0	0.0%	5.0%	5.0%		
	1-4days	Count	0	9	39	48		
		%	0	15.0%	65.0%	80.0%		
	4-8days	Count	0	3	6	9		
		%	0	5.0%	10.0%	15.0%		
	Total	Count	0	12	48	60		
		%	0	20.0%	80.0%	100.0%		
Positive	>15days	Count	5	4	3	12	15.66	0.016*
		%	8.3%	6.7%	5.0%	20.0%		
	1-4days	Count	0	4	1	5		
		%	0.0%	6.7%	1.7%	8.3%		
	4-8days	Count	6	11	0	17		
		%	10.0%	18.3%	0.0%	28.3%		
	9-14days	Count	4	10	12	26		
		%	6.7%	16.7%	20.0%	43.3%		
	Total	Count	15	29	16	60		
		%	25.0%	48.3%	26.7%	100.0%		

*significant

Covid positive patients also have various spectrum of olfactory dysfunction, In COVID 19 positive patients 15(25%) had Anosmia, 29 (48.3%) had Hyposmia, 16 (26.7%) had no loss of smell. Among COVID negative/suspects patients most of the patients patients had no loss of smell about 48 (80%), 12(20%) patients had Hyposmia. Study shows significant associations of olfactory dysfunction in COVID positive patients with p-value-0.016* and chi square value 15.66.

DISCUSSION

We have observed 120 patients with COVID 19 infection and COVID negative/Suspect, we compared olfactory and gustatory function in COVID POSITIVE and COVID negative/suspects and there effects on quality of life by using psychophysical test called Short version of questionnaire of olfactory disorders-negative statements of patient (sQOD-NS).

In a study total 60 COVID-19 positive patient and total 60 COVID-19 negative/suspect we're enrolled, Among COVID-19 positive patient, males were 43 and females were 17 and among 60 patients of COVID negative/Suspect status, males were 39, females were 21.all these above subjects were followed up after onset of Influenza like illness symptom onset over 3 weeks, Covid positive patients also have various spectrum of olfactory dysfunction, In COVID 19 positive patients 15(25%)had Anosmia, 29 (48.3%)had Hyposmia, 16 (26.7%) had no loss of smell. Among COVID negative/suspects patients most of the patients patients had no loss of smell about 48 (80%), patients No one had Anosmia, 12(20%) patients had Hyposmia .on evaluation found that most of the COVID positive

had taken 1-2wk and even more than 2wk to recover the smell sensations after symptom onset but most of the COVID negative/suspect patients had taken less than 1wk to recover the smell sensations.

COVID positive patient were having maximum score of short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) comparative to COVID negative/suspect patients, validated short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) by the National Health and Nutrition Examination Survey each and every question has significant associations in COVID positive patients than COVID negative/suspect patients

Among COVID positive patients Loss sensations seen) and among COVID negative/suspect patients loss of taste seen in 9patients (7.5%), No loss of taste seen in 51 patients (42.5%) In Iran, 48.23% of COVID 19 patients reported anosmia/ hyposmia. The onset of anosmia was sudden in 76.24% of patients. A total of 83.38% of these patients were having concomitant dysgeusia (decreased taste sensation) and anosmia.

The mean duration of anosmia in our patients was 7.8 (± 5) days. Anosmia/hyposmia resolved within 1 week in 65% of patients (n = 44) and within 2 weeks in 32% of the patients. However, hyposmia lasted beyond 2 weeks in 2 patients. The patients called back and informed us of the resolution of anosmia at 1 month. Lechien *et al*., observed the recovery of anosmia in 72.6% of their patient population within the first 8 days of the disease. The early olfactory recovery rate was 44.0% [4] Lee *et al*., also found the duration of anosmia to be 7 (± 4 days).

Olfactory and gustatory disorders are often associated with Upper respiratory tract infections; Evidence shows that they can be present in COVID 19 patients without concomitant nasal obstruction or congestion. Olfactory and gustatory dysfunctions affect about 41% and 38% patients with COVID 19 respectively.

Our study confirms that these dysfunctions are more common in COVID-19 positive patients compared to COVID-19 negative/suspects. This study also shows that the time taken for recovery is significantly higher in COVID-19 positive patients compared to COVID negative/suspects.

Over the past few weeks, an increasing number of otolaryngologists reported sudden anosmia or hyposmia as concurrent symptoms of COVID-19 infection. In these patients, the diagnosis of COVID-19 could be missed, because these symptoms were not known to be specific. As a result, the patients were not isolated and the spread of the virus.

CONCLUSION

We concluded that patients with COVID 19 positive status had severe spectrum of olfactory dysfunction like anosmia, hyposmia and they will have long recovery time compared to COVID negative /suspect patients .Taste perception was more impaired in COVID positive patients compared to COVID negative /suspects. Covid positive patients had higher sQOD-NS score compared to COVID negative patients and significant associations are seen. Hence these symptoms can aid in diagnosis of COVID-19 which can be further confirmed by confirmatory tests.

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