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## Original Research Article

## A cross-sectional study of thyroid profile, Anti-TPO and iron levels with uric acid of melasma cases in tertiary hospital, Bhopal

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## ABSTRACT

**Background:** Melasma, also called 'chloasma', is a common skin condition of adults in which light to dark brown or grayish pigmentation develops, mainly on the face. Although it can affect both genders and any race, it is more common in women. Melasma is an acquired pigmentary disorder described as symmetrical blotchy or splotchy hyperpigmented macules and patches.<sup>1</sup>

**Objectives:** The aim of this study was to investigate thyroid profile with anti TPO and iron, uric acid level, in male and female patients.

**Materials and Methods:** It is a cross-sectional observational study done on 76 females and 25 male who were diagnosed with melasma and thyroid profile with anti TPO, serum iron and uric acid levels were measured.

**Results:** In our study females were more affected than males. In females Mean  $\pm$  SD value of serum TSH ( $5.1 \pm 2.51$ ) and anti-TPO ( $11.2 \pm 3.1$ ) levels were increased when compared to males ( $4.9 \pm 2.54$ ) and ( $9.2 \pm 1.9$ ). Serum iron value was low in females ( $83.7 \pm 30$ ) than males ( $90 \pm 29$ ). All biochemical parameter were not significant but anti TPO and FT3 showed significant ( $P < 0.001$ ) in female with compared to male. Serum uric acid ( $3.56 \pm 0.77$ ) and serum iron ( $83.7 \pm 30$ ) Mean  $\pm$  SD value was low in melasma females than males which is not significant. Females Mean  $\pm$  SD value of T3 ( $1.30 \pm 0.62$ ) and T4 ( $6.8 \pm 1.9$ ), FT4 ( $1.2 \pm 0.44$ ) were non significance showed than compared to males and not significant to males T3 ( $1.33 \pm 0.66$ ) and T4 ( $7.1 \pm 1.6$ ), FT4 ( $1.3 \pm 0.67$ ) respectively.

**Conclusion:** Melasma is more severe in females than males. Thyroid profile is not the accurate parameter but anti TPO, and iron level are predictive marker of melasma.

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## 1. Introduction

Chloasma is a localized chronic acquired hypermelanosis, common in adult women and which has an important impact on their life quality. Its pathology is unknown, despite some recognized triggering factors.

Melasma also called chloasma and "the mask of pregnancy," is a wide spread, but I am not agree that is chronic cutaneous discoloration typically affecting females

of childbearing age. Melasma is clinically recognizable in three typical patterns:-Centro facial, malar, and mandibular.

Melasma may present as freckle-like spots or larger flat brown patches. Several distinct patterns include Centro-facial pattern involving forehead, cheeks, nose and upper lips, malar pattern involving cheeks and nose, less common patterns include mandibular pattern, involving ramus of the mandible, lateral cheek and brachial pattern.<sup>1</sup>

It is triggered by several factors including sun exposure, genetic influences, and female sex hormones. The pathology of melasma extends beyond melanocytes and recent

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literature points to interactions between keratinocytes, mast cells, gene regulation abnormalities, neovascularization, and disruption of basement membrane.<sup>2</sup>

Thyroid disorders were the systemic disease associated with melasma. Thyroid imbalances have a probable effect on onset of melasma. Hormonal and environmental factors like hormone receptors, blood vessels, sebaceous gland density and activity, phototoxicity, and antioxidants may be involved so that certain areas of the face are predisposed to develop melasma. It has been demonstrated that the melanocortin system interacts with the hypothalamic-pituitary-thyroid axis pigmentary changes may occur in thyroid diseases.

Thyroid diseases are, debatably, amongst the commonest endocrine disorders worldwide. India too is not an exception. Thyroid disorders are known to involve all the organ systems of the body and the skin is no exception, ACTH and MSH can activate melanocortin receptors in melanocytes, inducing melanogenesis. Thyroid autoimmunity and thyroid hormone abnormalities might also play a role in the pathogenesis.<sup>3</sup>

It was observed that melasma has traditionally been considered to be a pigmentation disorder of the female sex, but the occurrence in men is not uncommon. It appears to affect dark-skinned men of Asian and African-American origin more frequently than previously thought. The etiopathogenesis of melasma in men is similar to that of women, except for hormonal factors, which are more prevalent in women. Malar melasma is most common in men.<sup>4</sup>

Melasma is a common skin condition that affects both men and women. Melasma is less common in men, but it negatively affects the quality of life in men as much as it does in women. Seray Külcü et al. discusses important clinical aspects of melasma in men. They showed that thyroid autoimmunity and thyroid hormone abnormalities might also play a role in the pathogenesis. They suggested that thyroid hormones induce production of inflammatory cytokines. Higher circulating levels of pro-inflammatory cytokines have been shown in patients with hyperthyroidism.<sup>5</sup>

In women, hormonal factors, such as pregnancy, oral contraceptive pills, hormonal therapy, and mild ovarian dysfunction, are considered to be some of the most common etiological factors in the development of melasma. Hormonal imbalances between estrogen and testosterone might play a role in the development of melasma in men.

Estrogen increases melanin synthesis by stimulating the activity of tyrosinase enzyme. Further, it increases the extrusion of melanin from the cells. Several studies have found increased estrogen levels in women with melasma. Tadokoro et al. 32 indicated that testosterone affects human melanocytes by reducing the level of intracellular cyclic adenosine monophosphate and tyrosinase activity, thereby

decreasing melanogenesis. That also causes melisma.<sup>6</sup>

Melasma is a common, acquired facial skin disorder, mostly involving sun-exposed areas like cheeks, forehead and upper lip. Melasma occurs in both sexes, although almost 90 percent of the affected are women. The etiology is still unknown. The most important ones are sun-exposure and genetic factors in both sexes, while hormonal activity has more important role in females.

Also in India, it was demonstrated that average age and disease duration were similar between men (33.5 and 3.5 years) and women (31.5 and 3.1 years). The main risk factors identified for men were: sun exposure (48.8%) and family history (39.0%). For women, risk factors were associated with pregnancy (45.3%), sun exposure (23.9%) and use of combined oral contraceptives (COC) (19.4%).<sup>7</sup>

Melasma is a very common cutaneous disorder, accounting for 0.25 to 4% of the patients seen in Dermatology Clinics in South East Asia, and is the most common pigment disorder among Indians. The disease affects all races, but there is a particular prominence among Hispanics and Asians. Although women are predominantly affected, men are not excluded from melasma, representing approximately 10% of the cases.<sup>8</sup>

## 2. Materials and Methods

This study was conducted as a hospital based on observational cross-sectional study at Department of Dermatology in collaboration with department of Biochemistry, LNMC and associated J.K. Hospital, Bhopal during the study period of 18 months i.e. from 1st March 2019 to 30th August 2020. We included patients who have melasma as a case group. Person with a history of thyroid disease and hormone usage therapy, or pregnancy were excluded. A detailed history regarding the demographic profile, medical history, and medical examination was performed in both cases after taken a written consent form. A total of 100 cases of clinically diagnosed melasma patients of the group (18-65yrs.) constituted the subject material for the present study.

The protocol was obtained from the ethical committee of this study. Keeping this in view, we hypothesized that thyroid profile anti-TPO are more often positive in patients of melasma with iron and uric acid. All the patients were subjected to investigations including thyroid profile, anti-TPO, serum iron and uric acid in NABL accredited central pathology lab.

Serum was separated and stored. We conducted this study control pathology lab in J.K. Hospital and Research center. We estimated thyroid profile in fully automated analyzer based on quantitative enzyme-linked fluorescent immunoassay (ELFA). We calculated serum iron in ferrozin colorimetric method. We estimated uric acid in urease method. Anti TPO estimation method of ELISA with Bio detect Elisa Kit, Uses Microplate ELISA method.

### 2.1. Statistical analysis

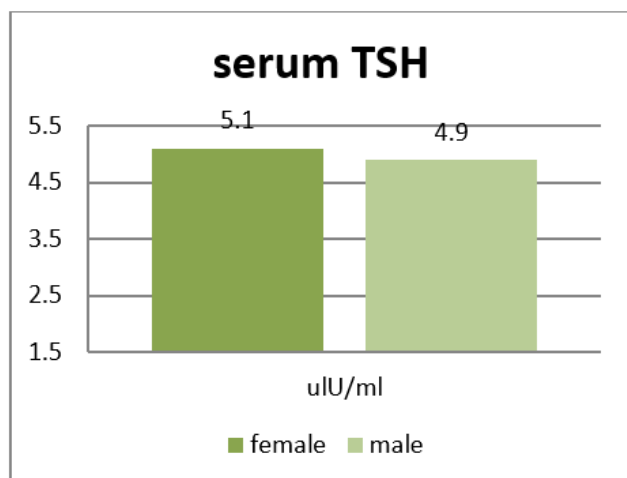
Data was compiled using MS Excel and analyzed using software Graph pad prism (9.12). Categorical data was expressed as mean and standard deviation. Continuous variables between cases and controls were compared using Chi-square test independent t test. P value less than 0.05 was considered statistically.

### 3. Result

The study comprised of 100 patients of melasma; the demographic features of which are given in Table 1.

Rashmi Sinha study confirm that the possible inter-relationship between purine nucleotide metabolism and thyroid disorders. Many biochemical pathways in the body can be affected by disturbance of thyroid hormones level, uric acid is one of these biochemical pathways. The hypodynamic state of the circulatory system in hypothyroidism that causes the elevation of uric acid level as in this study.<sup>9</sup>

Hyperuricemia was revealed as an important possibly independent risk factor for new-onset kidney disease. Dermatologists' awareness and knowledge about hyperuricemia may favor a faster diagnosis of this metabolic disorder based on skin lesions.<sup>10</sup>

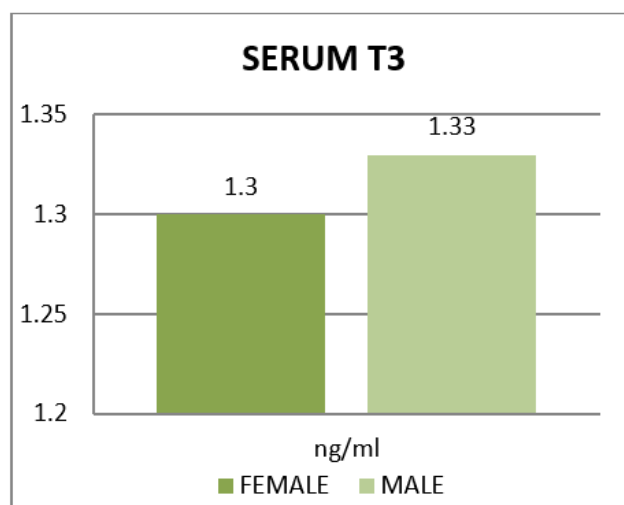


Graph 1: Serum TSH level among in cases gender-wise

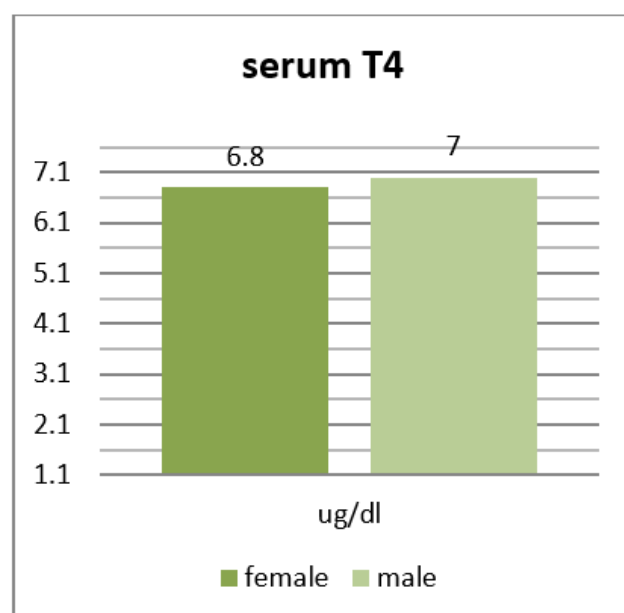
When comparing means of parameters serum TSH between females and males cases student's t-test, showed a not significant ( $p < 0.7485$ ) difference. But higher in females cases.

When comparing means of serum T3 biochemical parameters between cases female and males student's t-test, showed a not significant ( $p < 0.8486$ ) difference but higher in male.

When comparing means of serum T4 level between cases males and females with student's t-test, showed not significant ( $p < 0.6833$ ) difference.



Graph 2: Serum T3 level in males and females



Graph 3: Serum T4 level in cases gender wise parameters

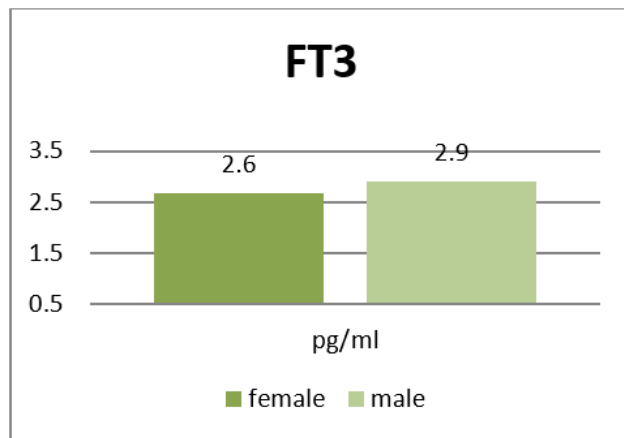
When comparing means of biochemical parameter serum FT3 between males and females with student's t-test, showed a significant ( $p < 0.0367$ ) difference and higher in males.

When comparing means of biochemical parameters between cases males and female student's t-test, showed not significant ( $p < 0.6478$ ) difference. Male showed higher mean level.

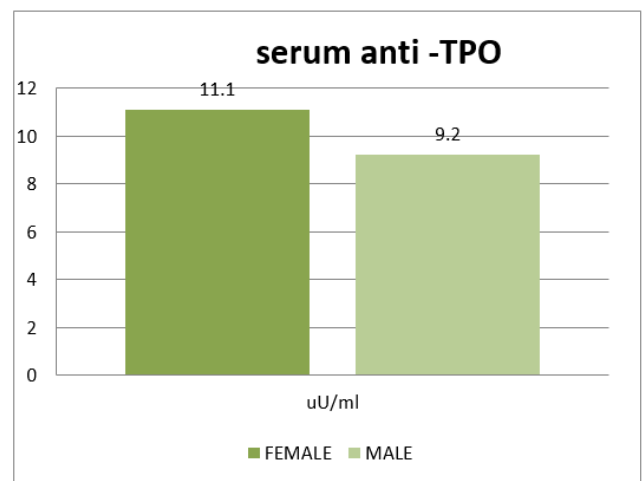
When comparing means of serum ANTI TPO level between males and females cases student's t-test, showed a significant ( $p < 0.0011$ ) difference and females showed higher than males.

**Table 1:** Gender wise distribution of melasma subject and their relation with thyroid disorders

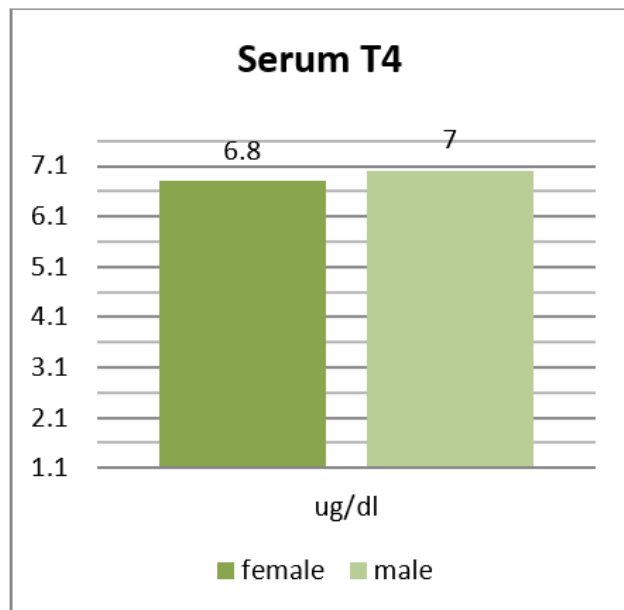
S.No	Parameter	Range	Female group (median $\pm$ SD)	Male group (median $\pm$ SD)	p Value	Test
1	T3	0.55-1.60 ng/mL	1.30 $\pm$ 0.62	1.33 $\pm$ 0.66	0.8486	Non Significance
2	T4	4.66-9.33ug/dl	6.8 $\pm$ 1.9	7.1 $\pm$ 1.6	0.6833	Non Significance
3	TSH	0.25 - 5	5.1 $\pm$ 2.51	4.9 $\pm$ 2.54	0.7485	Non Significance
4	Anti-TPO	<7.0IU/mL	11.2 $\pm$ 3.1	9.2 $\pm$ 1.9	0.0011	Significance
5	FT3	2.6-5pg/dl	2.6 $\pm$ 0.47	2.9 $\pm$ 0.42	0.0367	Significance
6	FT4	0.89-1.76ng/dL	1.2 $\pm$ 0.44	1.3 $\pm$ 0.67	0.6478	Non Significance
7	Uric Acid	2.8-7mg%	3.56 $\pm$ 0.77	3.59 $\pm$ 0.87	0.9167	Non Significance
8	Serum Iron	50-165 $\mu$ g/dl	83.7 $\pm$ 30	90 $\pm$ 29	0.3158	Non Significance



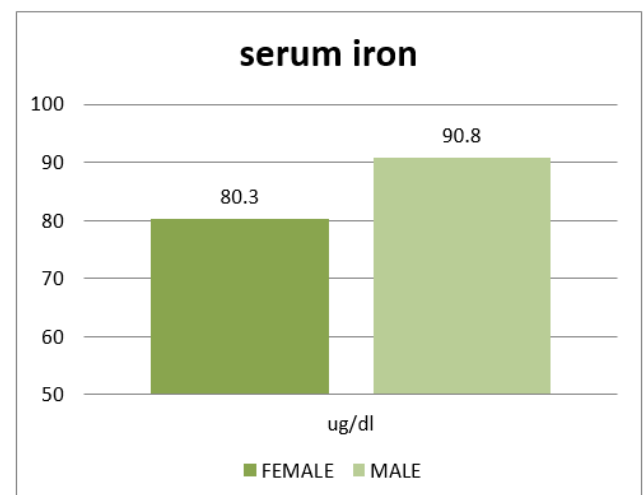
Graph 4: Serum FT3 level in cases gender wise biochemical parameters



Graph 6: Serum anti TPO level based on gender wise among cases

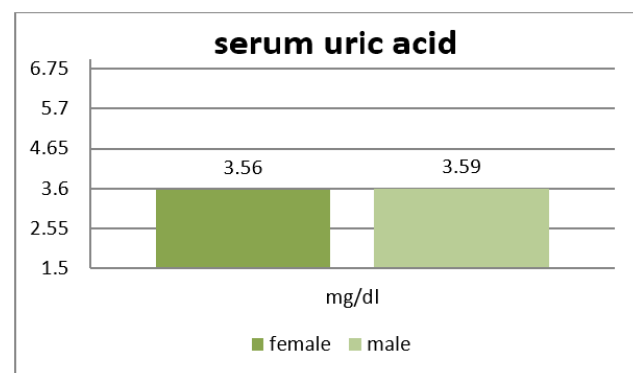


Graph 5: Serum FT4 level in cases gender wise biochemical parameter



Graph 7: Serum iron level in cases gender wise biochemical parameter

When serum iron means comparing between males and females cases student's t-test, showed not significant ( $p < 0.3158$ ) difference. But serum iron level higher in males.



Graph 8: Serum uric acid level in cases gender wise

When comparing means of uric acid gender-wise in cases student's t-test, showed not significant ( $p < 0.9167$ ) difference. Even not means significance differences.

In our study female are more effective than male, female serum TSH ( $5.1 \pm 2.51$ ) and anti-TPO ( $11.2 \pm 3.1$ ) level are increase when compare to male ( $4.9 \pm 2.54$ ) and ( $9.2 \pm 1.9$ ) but serum iron value was low in females ( $83.7 \pm 30$ ) than males ( $90 \pm 29$ ). All biochemical parameter was not significant but anti-TPO and FT3 showed significant ( $P < 0.001$ ) in female with compared to male. Serum uric acid and serum iron value is low in melasma females ( $3.56 \pm 0.77$ ) ( $83.7 \pm 30$ ) then male which is not significant similarly T3 ( $1.30 \pm 0.62$ ) and T4 ( $6.8 \pm 1.9$ ), FT4 ( $1.2 \pm 0.44$ ) were showed not significant to male T3 ( $1.33 \pm 0.66$ ) ( $1.30 \pm 0.62$ ) and T4 ( $7.1 \pm 1.6$ ), FT4 ( $1.3 \pm 0.67$ ) respectively.

#### 4. Discussion

In Tunisia, among 197 patients with melasma, nine (5%) were men with skin types IV and V.<sup>11</sup> A cross-sectional study in Southern Brazil identified melasma in 10.7% of 224 pregnant women.<sup>12</sup> In Iran, melasma was identified in 16% of women; in Morocco, in 37%; and in Pakistan, in 46%.<sup>13</sup> This strengthens the evidence of hormonal involvement in the genesis of the disease, since high levels of estrogen, progesterone and melanocortin are possible triggering factors of melasma during pregnancy. Also in India, it was demonstrated that average age and disease duration were similar between men (33.5 and 3.5 years) and women (31.5 and 3.1 years). The main risk factors identified for men were: sun exposure (48.8%) and family history.<sup>14</sup>

The prevalence of melasma varies between 1.5% and 33.3% depending on the population. Melasma can also occur in men, though less common. Sarkar et al. conducted an etiological and histological study in Indian males with melasma and found that men represent 20-25.83% of the cases. In men, the malar pattern is more common than the

centrofacial and mandibular patterns.<sup>15</sup>

We included 100 cases with confirmed melasma 75 females and 25 males observed thyroid biomarkers with iron and serum uric acid. The mean age of cases as well as 18-50 years and majority of participants were females irrespective of presence. Our study were supported of Rashmi Sarkar findings.<sup>15</sup>

Study by Biyani VV et al.<sup>16</sup> studied 100 patients among which 68 were males and 32 females. 49% of the patients had hyperuricemia. Similar results were concluded in studies by Millinois et al. and Patil T et al. Uric acid levels were significantly higher in males than females.<sup>17</sup>

Achar A, tried to find an association with endocrinal diseases and observed that 20 of had hypothyroidism and noticed 6.41% of our patients having thyroid dysfunction.<sup>18</sup>

Serum levels of TSH, anti-TPO, and antithyroglobulin antibody were significantly higher in patients with melasma than those without melasma. Moreover, these differences were more severe among women with melasma.<sup>19</sup>

Thyroid hormone act in hemoglobin synthesis in adults by affecting hematopoietic process, hypothyroidism results in anemia. Iron deficiency anemia which is quite common in Indian subcontinent should be clarified with specific clinical condition that results in iron deficiency.<sup>20</sup>

Engler H, Riesen WF, Keller B In autoimmune hypothyroidism a marked variability in anti-TPO levels was noted. Some patients showed a clear decrease in anti-TPO levels during T4 substitution whereas in others no consistent changes were observe.<sup>16</sup>

Babaienajad Ahahla at al observed low serum iron levels 8.6% of patient's abnormal ferritin levels in melisma.<sup>21</sup>

Iram Qazi et al. also showed patients with melasma had low body Iron stores compared to the control population indicating a possible role of iron deficiency in the etiopathogenesis of melisma.<sup>22</sup>

In our study, we found that about 80% of women and 20% of men have melasma. Most studies conducted in India showed almost similar results. Studies by Achar and Rathi,<sup>12</sup> Krupa Shankar et al.,<sup>13</sup> and Sarkar et al.<sup>6</sup> showed 24.4%, 19.9%, and 25.8% involvement of Indian males with melasma, respectively.

#### 5. Conclusion

In our study female are more affective than males. Serum TSH ( $5.1 \pm 2.51$ ) and Anti-TPO ( $11.2 \pm 3.1$ ) level are high but serum iron value was low in females than males. All biochemical parameter were not significant but anti-TPO and FT3 showed difference significant ( $P < 0.001$ ) in females as compared to males. Serum uric acid and serum iron value is low in melasma females than males. So anti-TPO and serum iron level is predicting bio marker of melasma.

## 6. Source of Funding

None.

## 7. Conflict of Interest

The authors declare no conflict of interest.

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