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Biochemical markers of ethnic Pakistanis: A correlation between genetic-aloofness and nutritional status affecting average age of each group

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The nutritional status and ethnic-aloofness (non mixed genomes owing to lack of cross marriages) might have direct impact on the average age and quality of health of the individuals belonging to different racial groupings. North Western region of Balochistan around Quetta, Pakistan, has diverse ethnic populations which afford a unique genomic pattern in addition to specific life style, pattern of eating, average age and quality of health. The biological correlation of this demography is expected to reflect on the overall quality of life of an individual. 100 subjects in each ethnic population belonging to middle social strata were sampled. Serum uric acid, urea and creatinine were determined using kits of Spinreact® according to the instructions of manufacturer. The blood parameters were correlated with body weight and age using standard statistical procedures. The subject from Pushtoons and Punjabis group were of significantly greater body weight compared to Baloch and Hazarajat (Persian-speaking) populations. The mean height of Pushtoons population was significantly greater than for all other groups. Uric acid level was greater in Pushtoons and Baloch compared to Hazarajat and no significant difference was observed between the Punjabis and Hazarajat. Serum urea was significantly greater in Hazarajat population compared to Pushtoons and Baloch, which had no difference from each other. The creatinine levels were very high in Punjabis population with respect to Hazarajat. There were positive differences in creatinine levels among Baloch and Pushtoons populations. It was found that genetic makeup based upon ethnic segregation is instrumental in varied level of various nitrogenous products in the blood. The variation in nutritional status (type of food intake) combined with environmental factors may additionally contribute towards the various nitrogenous products in the serum.

Key words: Ethnic-aloofness, Balochistan, serum uric acid, urea, creatinine.

INTRODUCTION

Emancipation of socioeconomic status of the societies over last several decades has induced a significant shift in eating behaviours from traditional high fibber's vegetative diet to more dairy based products originating from animals rather than plants. This has resulted into a variety of nutritional disorders and the major challenges for today's nutrition scientists to discover the means to control such misgivings (Cuco et al., 2002). The habitual

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consumption of this dietary blueprint has link to an enhanced threat of developing chronic illnesses such as cardiovascular disorder, obesity and cancer (Bingham, 1999; Cuco et al., 2002). Diet, particularly high protein intake, is the major environmental determinant in the formation of uric acid stones (Remer and Manz, 1994). There is also the evidence linking uric acid levels in blood to atherosclerotic process that is the formation of thrombosis (Becker, 1993). Hyperuricemia is related to high risk for cardiovascular diseases (CVD), for example hypertension, obesity, dyslipidemia, hypoinsulinemia and inactive life style (Culleton et al., 1999; Freedman et al., 1995; Lee et al., 1995; Persky et al., 1979). High serum uric acid levels robustly reflect and may even cause oxidative stress, insulin resistance, inflammation and metabolic syndrome, which are risk factors for the progression of liver diseases as well as aging (Afzali et al., 2010; Alimonda et al., 2009).

In combination with genetic and environmental factors, uric acid is capable of causing significant health complications like kidney stones and gout (Kuwano et al., 1996; Pyorala et al., 1987; Visy et al., 1991). A number of epidemiological data have revealed the linkage of hyperurecemia with the transformation and affluence on everyday life and greater prevalence of gouty arthritis in Asian populations (Darmawan et al., 1992; Lin et al., 2000). Serum uric acid has correlation not only to risk of gout, but also with hypertension, chronic heart failure, obesity and diabetes mellitus (Alderman 2002; Breckenridge 1966; Goldbourt et al., 1980; Hall et al., 1967; Herman and Goldbourt 1982; Li et al., 1997; Mikkelsen 1965; Prior et al., 1966; Tuomilehto et al., 1988; Yano et al., 1977). However, the exact role of serum uric acid in the pathogenesis of these diseases is still speculative.

Serum uric acid level is affected equally by heritable and environmental factors and is correlated to biological parameters such as gender, age, body mass index and even the heights of individuals from diverse genetic background (Ahern et al., 1980; Goldbourt et al., 1980; Mikkelsen 1965; Tuomilehto et al., 1988; Yano et al., 1977). In relative epidemiological studies on Japanese men residing in Japan, Hawaii and California, it is documented that serum uric acid is considerably elevated in Japanese immigrants to Hawaii and California compared to Japanese living in Japan (Kagan et al., 1974; Yano et al., 1977). Investigation of serum uric acid level in Thai population in Bangkok and rural area have shown significant correlation between body mass index, height of the individuals and gender specificities (Pongpaew et al., 1977). It is worth to note that nutritional status of the population of this area is not comparable to western standards and hence has revealed significant variations in serum parameters particularly for females. In the present investigation, we attempted to study the role of serum uric acid, urea and creatinine in various ethnic groups in Pakistan and correlate the serum parameters with body weight, height and nutritional status across ethnicities.

MATERIALS AND METHODS

A randomized survey and sample collections was conducted in three districts of Balochistan. Healthy men and women volunteers form Quetta, Mastung and Pishin districts were selected with age range 25 to 45 years. The individuals were interviewed by a medical physician and a dental surgeon, using a standard questioner having information on age, gender, marital status, socio-economic status, ethnicity, physical activity, history of hypertension, diabetes, cardiovascular disease, osteoporosis and oral examination. Body mass index (BMI) was considered by obtaining weight of the subject in Kg and height in inches. Blood pressure was measured with manual sphygmomanometer (Yamasu Japan) according to a standardized protocol. 5 ml of blood was taken from each subject. The blood sample in the serum tube were allowed to clot for about 3 h and later centrifuged for 15 min for 1500 rpm. Serum urea, uric acid and creatinine were estimated in the sera by spinreact kits using semi-automated spinreact, spinlab (Vital scientific, Dieren Netherland).

RESULTS

The mean age of all the subjects of the four ethnic populations was 36±1.1 years. It was observed that the subjects of Hazarajat (Persian-speaking) population (38.47±1.44) year's were older and Baloch (34.38±0.97) subjects year's were younger compared to Pushtoons (35.69±0.82) years, and Punjabis (36.59±1.067) years (Table 1).

The mean weight of all the subjects of the four ethnic populations was 66±1.1 kg. The subjects of Pushtoons population showed (68.79±1.0 kg) the highest value. Almost in the same range was that of the Punjabis (67.08±1.1 kg). The subjects of Baloch (63.45±1.2 kg) groups were of lower body weight compared to Pushtoons and Punjabis populations. The weight of Pushtoons population was significantly higher compared to the Baloch and Hazarajat (63.52 $\pm$ 1.2 kg) populations. The weight of Pushtoons population was significantly high compared to the Baloch and Hazarajat populations. A statistically important difference (P= <0.001) was observed between the weight of Pushtoons, Baloch and Hazarajat populations while there was no statistically significant difference between Punjabis and Pushtoons populations (Table 1).

The mean of height of the sampled subjects was 65±0.5 inches whereas the individual mean of height in Pushtoons was 66.12±0.28 inches, 65.18±0.43 inches in Punjabis, 65.13±0.28 inches in Baloch and 64.78±0.45 inches in Hazarajat. A significant difference (P= <0.001) was observed between the height of Pushtoons population and Hazarajats (Figure 1 and Table 1).

The mean of BMI of all subjects was 23.94±0.44 kg/m^2: Pushtoons (23.67± 0.40 kg/m^2), Punjabis (23.67± 0.40 kg/m$^{2)}$, Baloch (22.84 ± 0.35 kg/m^2) and Hazarajat

Table 1. Summary of various parameters.

Parameter	Various ethnic population				
	Baloch (n=100)	Pushtoons (n=100)	Hazara (Persian) (n=100)	Punjabis (n=100)	Mean (n=400)
Age/ years	34.38±0.97	35.69±0.82	38.47±1.44	36.59±1.067	36±1.1
Weight/ kg	63.45±1.2*	68.79±1.0*	63.52 ± 1.2*	67.08±1.1	66±1.1
Height/ Inches	65.13±0.28	66.12±0.28	64.78±0.45	65.18±0.43	65±0.5
BMI/ kg/m^2	22.84±0.35	23.67± 0.40	22.58±0.34	23.67± 0.40	23.94±0.44
Diastolic Blood Pressure/ mmHg	82.63 ±0.99	82.59± 1.06	82.31 ± 1.42	83.92 ± 1.10	83± 1.2
Uric Acid/ mg/dl	4.47 ± 0.16^{ł}	4.45± 0.17^{ł}	3.7±0.16^{ł}	4.41±0.18	4.4 ± 0.17^{ł}
Serum Urea/ mg/dl	29.97± 0.87	29.13 ± 0.92	32.23 ± 1.17	27.87± 0.73	29.8 ± 0.92
Creatinine/ mg/dl	0.751±0.02	0.791± 0.02**$^{\phi\phi}$	0.699 ± 0.2$^{ł\phi\phi}$	0.875 ± 0.03**	0.779±0.02

*P= <0.001:Pushtoons-Baloch/Hazara; łP= <0.001: Hazara- Pushtoons/ Punjabis/ Baloch; ** P= <0.001: Pushtoons- Punjabis; ϕϕ P= <0.001: Hazara- Pushtoons.

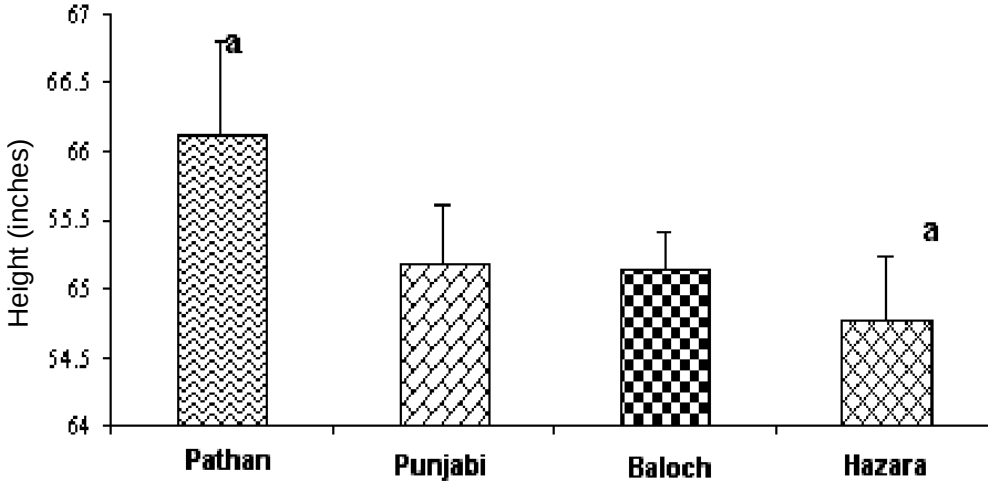

Figure 1. The mean values of height of sampled subjects of various ethnic populations. The same alphabets in different populations show the significant difference statistically.

(Persian) (22.58±0.34 kg/m^2). There was no noticeable dissimilarity in BMI of the subjects of various populations (Figure 2).

The mean diastolic blood pressure of all the subjects of the four ethnic populations was 83± 1.2 mm Hg. The mean blood pressure of each individual ethnic population was 82.59± 1.06, 83.92 ± 1, 82.63 ±0.99 and 82.31 ± 1.42 mmHg for Pushtoons, Punjabis, Baloch and Hazarajat populations, respectively. No significant variation was observed for comparison of the various ethnic populations (Table 1).

In all subjects, the mean of uric acid level was 4.4 ± 0.17 mg/dl, whereas for the individual population level were, 4.45± 0.17, 4.41±0.18, 4.47 ± 0.16 mg/dl for Pushtoons, Punjabis, Baloch respectively which is higher compared to Hazarajat subjects (3.7±0.16 mg/dl). The Hazarajat population has lower level of uric acid as compare to other ethnic groups. A statistically significant difference was observed between the uric acid level of Hazarajat subjects with respect to Pushtoons, Punjabis and Baloch population (P = <0.001) (Figure 4).

The serum urea level in all four populations was in 29.8 ± 0.92 mg/dl with a mean values of 29.13 ± 0.92, 27.87± 0.73, 29.97± 0.87 and 32.23 ± 1.17 mg/dl for for Pushtoons, Punjabis, Baloch and Hazarajat populations, respectively. No significant variation was observed for the comparison of the various ethnic populations (Figure 5).

The creatinine level in all four populations were 0.791± 0.02 mg/dl in Pushtoons, 0.875 ± 0.03 mg/dl in Punjabis, 0.751±0.02 mg/dl in Baloch and 0.699 ± 0.2 mg/dl in Hazarajat. A significant difference was observed between the creatinine levels of various populations. Statistically

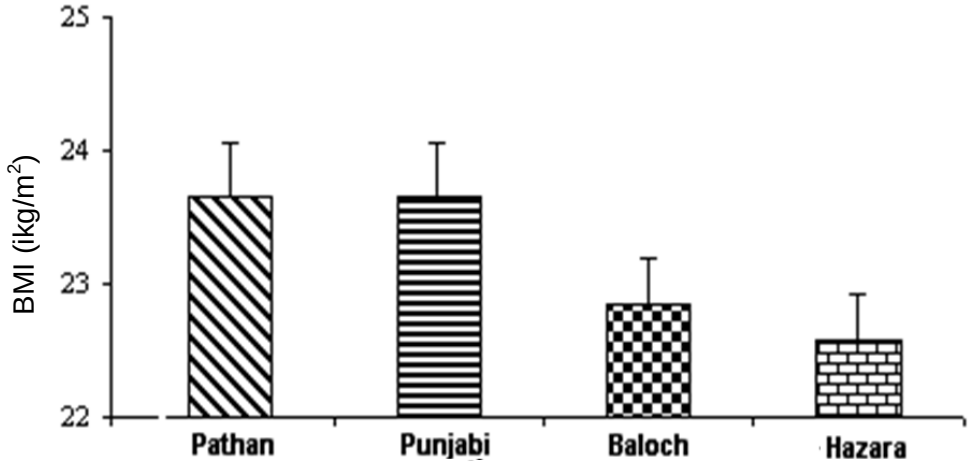

Figure 2. The mean values of BMI (kg/m2) of sampled subjects of various ethnic populations

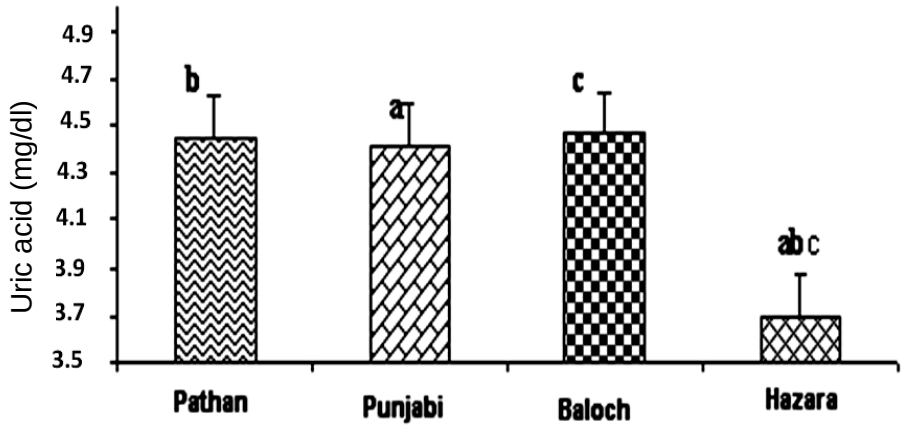

Figure 3. The mean values of uric acid (mg/dl) of sampled subjects of various ethnic populations. The same alphabets in different populations show the significant difference statistically.

difference was observed between the creatinine level of Punjabis and Pushtoons subjects and among the Pushtoons and Hazarajat subjects (P = < 0.001) (Figure 5).

DISCUSSION

The North western region of Balochistan, particularly the district of Quetta, Pishin and Mustang constitute the region with diverse populations of Pushtoons, Baloch, Punjabis and Hazarajat (Persian-speaking) ethnic groups. These ethnic groups in general maintain their traditional life styles; cross-marriages are extremely rare or non-existing and have different nutritional patterns; however the climatic conditions of their lives are generally the same. Their genomic makeup and life styles present a specific adaptation to the same environment at biochemical, physiological and molecular levels, hence presents a unique opportunity to study the effects of diet on their age, health and life expectancy.

In the present study, the main focus was on the protein metabolism. It is pertinent to note that this particular climate affords abundant livestock and consequently heavy meat consumption is induced in various populations. Therefore, these localities may be taken as suitable laboratories for the assessment of the effects of heavy protein consumption. It is known that ingestion of large amount of protein food markedly increases the endogenous output of uric acid (Lewis and Gardner, 1960), thus we have very simple and accurate method to monitor the effects of heavy protein diet on overall

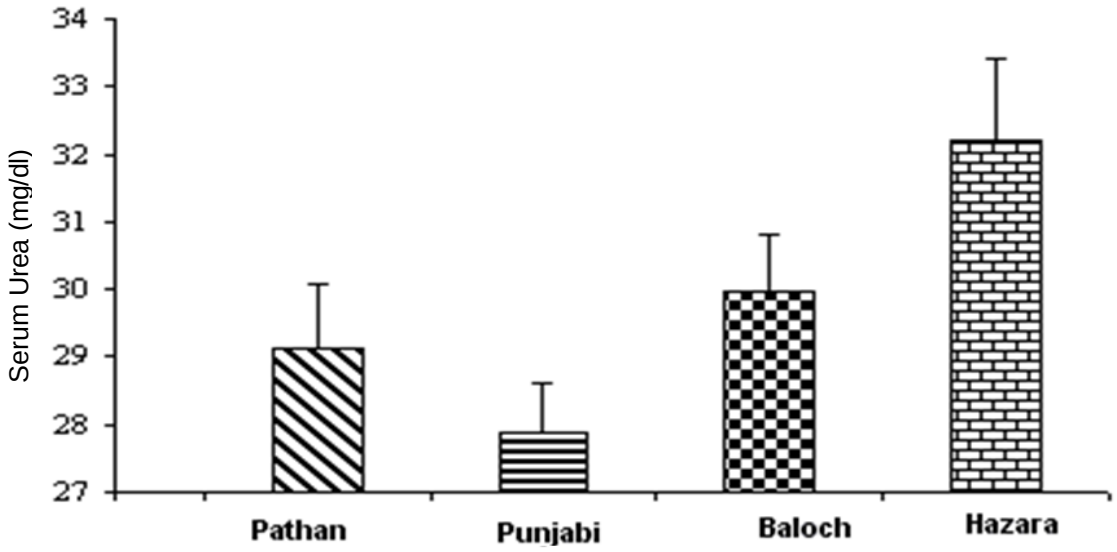

Figure 4. The mean values of urea (mg/dl) of sampled subjects of various ethnic populations.

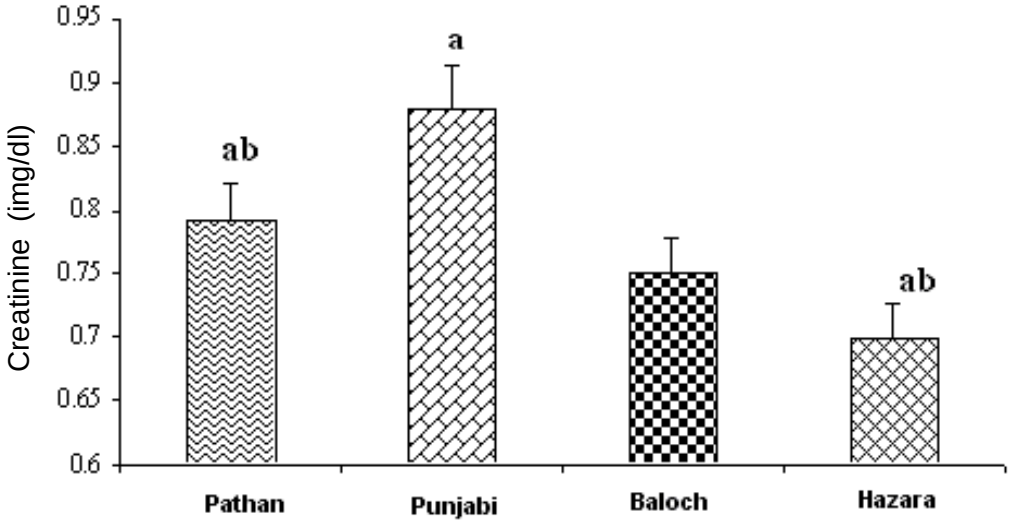

Figure 5. The mean values of creatinine (mg/dl) of sampled subjects of various ethnic populations. The same alphabets in different populations show the significant difference statistically.

quality of the life of a person in these ethnicities.

The Pushtoons and Punjabiss are statistically significantly greater in weight and taller in height compared to the Hazarajat and Baloch subjects (Figure 1 and Table 1). The differences among Punjabiss and Pushtoons were statistically non significant. Though the BMI was not statistically different among different ethnicities but it did indicate a trend of being lower among Hazarajat and Baloch compared to Pushtoons and Punjabis (Table 1).

Weight of the individuals could be correlated to height in ethnic Punjabis and Hazarajat but not in Baloch and Pushtoons (Figure 2, Table 1). The weight of an individual in general could also be correlated with BMI, so was the case among these ethnicities except Baloch: among them it was very difficult to find a correlation for height parameter either to the body weight or BMI (Figure 2, Table 1). These discrepancies could be understood if we take into account the genetic makeup of these ethnicities. It is reported (Li et al., 1997) that height is mainly dependent upon genetic makeup in most populations. Thus taller heights of Pushtoon population compared to short stature of Hazarajat and Baloch subjects are the expression of their genetic makeup rather than the nutritional status.

It is also known that serum uric acid levels of an

individual are affected both by genetic and environmental factors (Li et al., 1997). We found significantly lower serum uric acid level in Hazarajat population compared to the other ethnicities (Figures 3 and 4). In Pushtoon-population, uric acid is positively correlated with urea, which is a known promoter of renal elimination of uric acid (Garrel et al., 1990). Also, in Hazarajat subjects a positive correlation between serum urea and uric acid level existed (Figure 3, 4 and Table 1). In Hazarajat and Baloch populations with the highest weight group that is > 75 Kg showed significantly greater level of uric acid compared to other individuals body weight. It is likely that obesity which is the result of fat-deposition creates sluggish trend in the elimination of uric acid. The lower uric acid in Hazarajat subjects may not be due to the dietary factors that could had been grasped from the collected data, rather it may a contrasting character of Hazarajat subjects stemming from genetic variation.

A correlation between the uric acid and creatinine was observed in the subgroup in Punjabis population. Subjects with the higher level of uric acid also had higher level of creatinine (Table 1). In Hangzhou urban population (Li et al., 2006), serum uric acid was significantly ($P < 0.001$) positively related with the creatinine. Serum urea although did not differ significantly. Nevertheless the values do indicate the variation of this parameter in different ethnic populations. The highest levels of the urea were observed in Hazarajat subjects, which in itself reflect the correlation of urea with uric acid in this ethnic group. In Baloch subjects, the high serum urea displaying individuals also had the highest level of creatinine, which was also significantly different from the individuals with lowest urea. This demonstrated intra group variation, very high meat eaters versus moderate consumers. Urea was positively correlated in Baloch and Pushtoons population with creatinine. In Baloch and Pushtoons populations, higher level of urea and creatinine were found. Two possible explanation of this phenomenon could be presented. First, conversion of uric acid into urea is not normal, and secondly creatinine elimination is comparatively sluggish. Thus biochemical parameters could be accounted for this expression. These data further elucidate that molecular and genetic mechanism might be the underpinning cause of this variation. Lower level of uric acid in Hazarajat and higher level of urea reflect the differences in biochemical mechanisms.

Creatinine level was higher in Pushtoons and Punjabis subjects compared to Hazarajat and similarly in Baloch population (Figure 5). In Hazarajat subjects, significantly low creatinine like that of uric acid demonstrates that creatinine is also converted into urea. This specific characteristic in the Hazarajat population is a genetic adaptation with subsequent proteomic expression in terms of the enzyme presence or absence.

In conclusion, it is tempting to hypothesize that genetic adaptation in Hazarajat ethnicity is responsible for variations in the serum concentration of various nitrogenous excretory products and the same unique genetic makeup pushes the average age (38.47±1.44) of this ethnicity higher compared to others like Baloch (34.38±0.97). It is now a well established biological theory that age is genetic (Kenyon 2010) though it is significantly influenced by environment. The adaptation in Hazarajat might have been due to pertinent nutritional factors or their interaction in the environment. These results provoke the need to assess these relationships in an extensive number of samples in each ethnicity and subsequently to validate their genomic and proteomic status.

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