Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jztq3v61

NUTRITIONAL AND EPIDEMIOLOGICAL CAUSES OF CHOLELITHIASIS: A CROSS SECTIONAL STUDY OF THE PARADIGM SHIFT IN THE RISK FACTORS AT KHYBER PAKHTUNKHWA

Dr. Fazia Ghaffar[1*]

[1*]Department Of Food & Nutrition Sciences University Of Peshawar Peshawar, Pakistan
Email: Faziaghaffar@Uop.Edu.Pk

***Corresponding Author:** Dr. Fazia Ghaffar
[*]Department Of Food & Nutrition Sciences University Of Peshawar Peshawar, Pakistan
Email: Faziaghaffar@Uop.Edu.Pk

ABSTRACT

Cholelithiasis has been regarded as one of the one of the most prevalent disease in the gastrointestinal disorders with a larger disease and emergency surgical burden. Many factors contribute to the development of gall stones; genetic and predominantly dietary and life style factors. No such studies have previously been done to determine the contributing risk factors of cholelithiasis in Khyber Pakhtunkhwa.

OBJECTIVES: (1). To determine the socio demographic risk factors of cholelithiasis at district Peshawar, Pakistan. (2). To analyze the dietary intake patterns, macronutrient densities of the diets, and physical activity patterns of the patients

METHODS: A total of 125 patients (being calculated at 95% confidence interval and 1% odds ratio) were recruited after written consents. Gall stones and their sizes were confirmed by ultrasonography. Socio demographic characteristics, anthropometric measurements, biochemical tests for liver function, clinical symptoms of malnutrition and disease associated were examined, Food frequency (daily, weekly, monthly) for different food groups were considered. Based on 72 hours recall mean macronutrient intakes, their percent contribution to daily energy intakes, and physical activity patterns were analyzed through WHO standardized IPAQ tool. Data was analyzed through SPSS for both continuous and categorical variables.

RESULTS: Among the study sample 95.4% patients were females, 97% married, 64% females, illiterate and 92% being housewives. Data of the male patients and husbands of the female patients collectively 53% were illiterate with low paid jobs while some were engaged in some government jobs. About 56% of the sample were living in extended family system, having children in the 5-9 category with the most common family size of 10-14 members (56%). About 55.2 % patients reported family history of gall stones. Majority of the patients had multiple stones of different sizes common being 2.2 cm. Clinical symptoms of iron and B complex vitamin deficiencies were commonly observed. Majority of the patients were referred to Ultrasonographic scans due to frequent GIT disturbances associated with gall stones. Mean age of the sample was 43.2± 21.93, while BMI (25.73 ±1.85), percent body fat (36.25±7.97) and % Visceral fat (9.45±19.76) showed a strong obesity and overweight trend (39.2% and 58.4% respectively) mainly the truncal obesity. The dietary frequency

showed an overall poor food choice with higher intakes of wheat-based staples, rice, lentils, beef, chapli kabab (the local beef Pattie with herbs, spices and deep fried in tallow) and intake of seasonal cooked vegetables was common. Alarmingly most of the sample consumed white sugar and hydrogenated fat (ghee) were common. The overall consumption of energy and energy nutrients were higher while dietary protein and fiber were quite low. Physical activity patterns showed 43.8% inactive, 46.2% minimally active and 49.6% patients had >5 sitting hours. The data showed strong associations with many of the study parameters.

CONCLUSION: The current study indicated age, being female gender, multiparity, larger family sizes, obesity, poor dietary choices, inactivity as the major contributing factors of cholelithiasis in this region.

KEY WORDS: Cholelithiasis, socio-demographic factors, dietary intake patterns, anthropometry, macronutrients, Physical activity

1. INTRODUCTION

Cholelithiasis or the formation of stones within the gall bladder or bile duct pose considerable medical burden globally. The aetiology and pathogenesis of gallstones is multifactorial with complex interactions of genetics, environment and life style; identifying the key risk factors is necessary for the better understanding of the disease and subsequent improvement of patient care [1]. The gallbladder stores bile acids and bile salts until they are needed to help digest fatty foods. Cholelithiasis is the condensation of cholesterol or bile pigments leading to the formation of solid crystal deposits in the gallbladder [2]. Gallstones are small and hard stones formed in the gallbladder. Gallstones range in size from as small as a grain of sand to as large as a golf ball. A person's gallbladder may have a single large stone, many small stones or both small and large stones [3]. Gall stones are mainly of three types. Cholesterol gall stones, pigment stones, and mixed stones. Cholesterol gallstone contain 90% cholesterol. Cholesterol is a fat and is insoluble in aqueous solution, so it is made soluble in the bile by combining it with bile salts and phospholipids. cholesterol gall stones are formed when the concentration of cholesterol increase to the extent that the bile cannot hold into its solution which leads to the formation of crystals that turn into stones. Pigment stones are made up to 90% bilirubin. Pigment stones are found when the bilirubin level in the bile increases as a result of destruction of the blood cells. Mixed stones are composed of cholesterol, bilirubin, calcium carbonate, calcium phosphate, and calcium palmitate [4, 5].

Some of the risk factors of gallstones disease are: increasing age, people are more likely to develop gallstones disease above age 40. women are known to be more prone to the disease as compared to men due to which high estrogen level is also known as one of the risk factors of gallstones [5]. Being overweight increases the cholesterol level in the body that leads to gallstones formation. rapid weight loss, fluctuating weight and gastric by-pass may also be positively associated with the disease [6, 7]. Diseases of small intestine like Crohn's disease, diabetes, paralysis, sickle cell anemia can also lead to gallstone disease. some of other risk factors are certain medications, lack of physical exercise, multiparity and family history [8-11].

This disease was first known to be the disease of west and developed countries but due to changes in food consumption it is now becoming more common in the developing countries [12]. The prevalence is different between countries as well as ethnic groups. it also differs in age and gender [13]. Due to changes in dietary intake and high intake of cholesterol and fatty foods, gall stone disease is becoming more common in Pakistan [14]. In Southern Punjab the prevalence for gall stones is 9.03% which is 4% in males and 14.2% in females. In this 9.03% females are 3.3 times more susceptible to develop gall stones as compared to males. Pigment stones are more common than the other stones [15]. Several studies reported that sex, age, body mass index, and race have been closely associated with gallstone diseases. However, in Khyber Pakhtunkhwa limited studies have focused on the risk factors gallstone diseases. Therefore, this study aimed to investigate and epidemiological characteristics and dietary

risk factors of gall stone disease in patients attending the surgical departments at two tertiary care units of Peshawar, Pakistan.

2. METHODOLOGY

2.1: Study Design and Sample

This case control cross sectional study was carried out at two tertiary care hospitals and ultrasonography clinics in District Peshawar, Pakistan. Sample size was calculated using an epi online calculator (www.openepi.com) after inserting 2.5 odds of other comorbidities at 95 % confidence interval the actual sample size was n=119, however for this study it was rounded to about 125 patients who were diagnosed with gallstones after confirmation by ultra-sonography. Each patient was investigated after taking written consent at the Surgical Department of Kuwait Teaching Hospital and Khyber Teaching Hospital and some Ultrasound clinics in the time period of May 2023 to October 2023. The study followed Helsinki guidelines and was approved by the relevant institutional regulations and standards of patients' confidentiality.

2.1.1: Inclusion Criteria: Participants with confirmed cholithiasis age >25 and <60 with no further hepatic complications, hepatitis, pancreatitis, severe cholecystitis, obstructive cholangitis, and recent history of other infections.

2.1.2: Exclusion Criteria: Patients who refused to participate, were to go through emergency cholecystectomy, were in disease related symptoms of pain, prolonged history of diabetes & hypertension (>10 years), were on psychotic drugs and had other comorbidities.

2.2: Data of Collection

A self-constructed and self-administered questionnaire was introduced to the subjects and were filled with the help subjects and their attendants. Data regarding socio demographic data, anthropometry data, bio chemical data, clinical data, physical signs for the good and poor nutrition, dietary data were collected. A 72 hours food intake record through recall was procured in order to ascertain nutrient intake patterns.

2.2.1: Socio Demographic Data

It included questions like gender, religion**,** education, occupation, marital status, parity, husbands 'education and occupation, age at marriage, type of family and size of family.

2.2.2: Anthropometry

It included age, weight, height, waist circumference, hip circumference, waist to hip ration, mid upper arm circumference MUAC as per recommended methods [16, 17]. Body Mass Index (BMI) was calculated through formula from the measurements of weight/height while body composition (total fat % and visceral fat %) was performed on Bioelectrical Impendence Analyzer (Body Composition Monitor, BF 508, Omron)

3: Bio Chemical Data

Laboratory tests for liver functions tests (bilirubin level, ALT and ALP), number and size of stones, were performed as per standard laboratory procedures

4: Clinical Data

Patients were assessed for the presence of symptoms of malnutrition and all the symptoms related to gallstones disease.

5: Physical activity

The International Physical Activity Questionnaires (IPAQ) [18] was used due to the section related to activities in and around the home, like housework, gardening, yard work, general maintenance work, and caring for the family and the sample we chose consisted mainly female patients who usually are more involved in domestic responsibilities. The respondents were analysed at three levels of IPAQ scoring i.e.,

1. Inactive (no activity or little activity that does not meet the criteria of 2 and 3)
2. Minimally active: Respondents who were involved in vigorous activities either on three or more days for a minimum of twenty minutes/ day or in moderate intensity activity or walking of at least 30 minutes/day.
3. HEPA Active: Respondents who were involved in vigorous activities for three days or a combination of vigorous, moderate intensity activities and walking or 1500 METs min /week on seven days of the week
4. Sitting time was calculated by excluding sleeping hours, & included TV watching & screen time, and home chore of light intensity (cooking, washing utensils, cleaning etc) while sitting.

5. IPAQ Scoring:

Metabolic Equivalents were calculated as per the following formulae
MET min/Week = Level of MET × min of activity × days per week
Walking (3.3 METs) = 3.3 × min of activity × days per week
Moderate Intensity (4.0 METs) = 4.0× min of activity × days per week
Vigorous Intensity (8.0 METs) = 8.0 × min of activity × days per week
Total METs min/Week = (Walk METs× min of activity × days per week) + (Moderate METs × min of activity × days per week) + (Vigorous × min of activity × days per week)

6. Dietary Data

6.1: Food Frequency

In order to analyze the general dietary intake patterns of the patients a pre standardized semi quantitative food frequency questionnaire was submitted. Food indigenously consumed were divided into ten food groups with subsequent sub categories. Data was recorded for frequency consumption per day, per week, and monthly basis.

6.2: Nutrient Intake Patterns

A 72- hours recall method was employed where the patients were asked about their food intake during the last three days in different meals. The intakes were analyzed for macro nutrient intakes through WinDiet software and means nutrients intakes were determined from the data.

7. Statistical Analysis

The data was statistically analyzed on IBM Statistical Package for Social Sciences (SPSS) version 23. Frequency, percentages, mean, standard deviation for all the qualitative and quantitative variables. In order to determine relationship different variables Pearson co efficient of correlation analysis was performed.

3. RESULTS AND DISCUSSION

3.1 DEMOGRAPHIC CHARACTERISTICS

The socio-demographic characteristics of the participants (Figure 1) sowed extended family system was the most common living style (56%) with 5-9 children in a nuclear section indicating greater parity (56%) followed by up to four children (36%). About 36% of the females' patients got married at the age of 16-19 years. The total family size showed a family structure of 10-14 members being the most common (56%) in the current study. The findings of the current study are in agreement with other studies who reported that urban setting, lower education, early marriages which prolong the

fertility period, number of children and multiple pregnancies are associated the with an increase in symptomatic cholelithiasis [19-24].

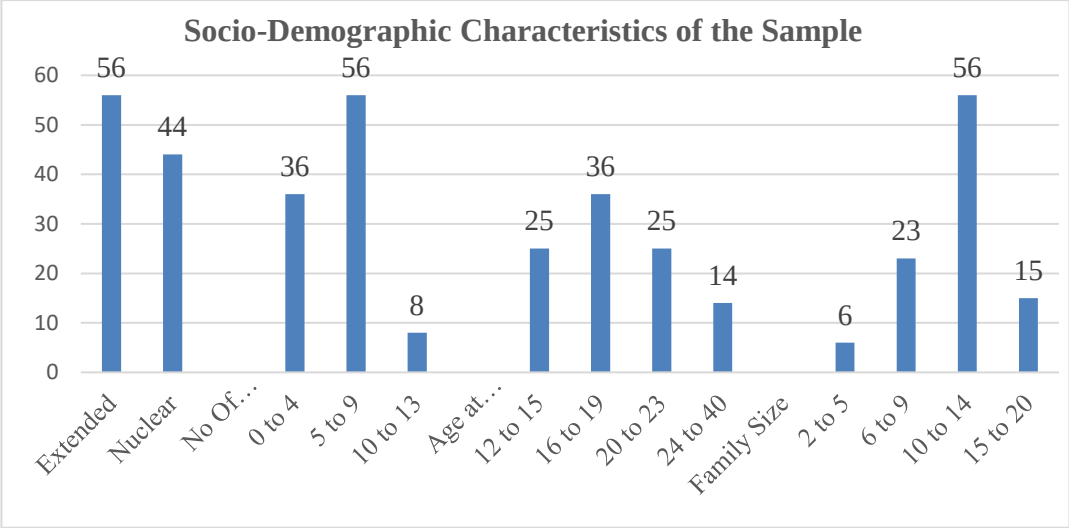

Figure 1: Socio-Demographic Characteristics of the sample

3.2: Marital, Educational & Occupational Background

Marital, educational, and occupational backgrounds are given in figure 2. About 97%. of the patients were married and 64% of the females did not attend any formal educational institutions, followed by 17% of schooling up to elementary level. The educational background of the husbands of the patients also followed the similar pattern with 53% illiterate, 24% elementary and 10% matriculate. These lower educational levels were evident from the 31% being jobless, 20% in low paid jobs and 23% were engaged in daily wage laboureres. Only !0 % of the men were in government jobs and 6% being school teacher's indicative of sedentary life style. These finding are in agreement with many such studies who found less education, lower family incomes may predispose the patients to poor dietary choices and life styles [22,23].

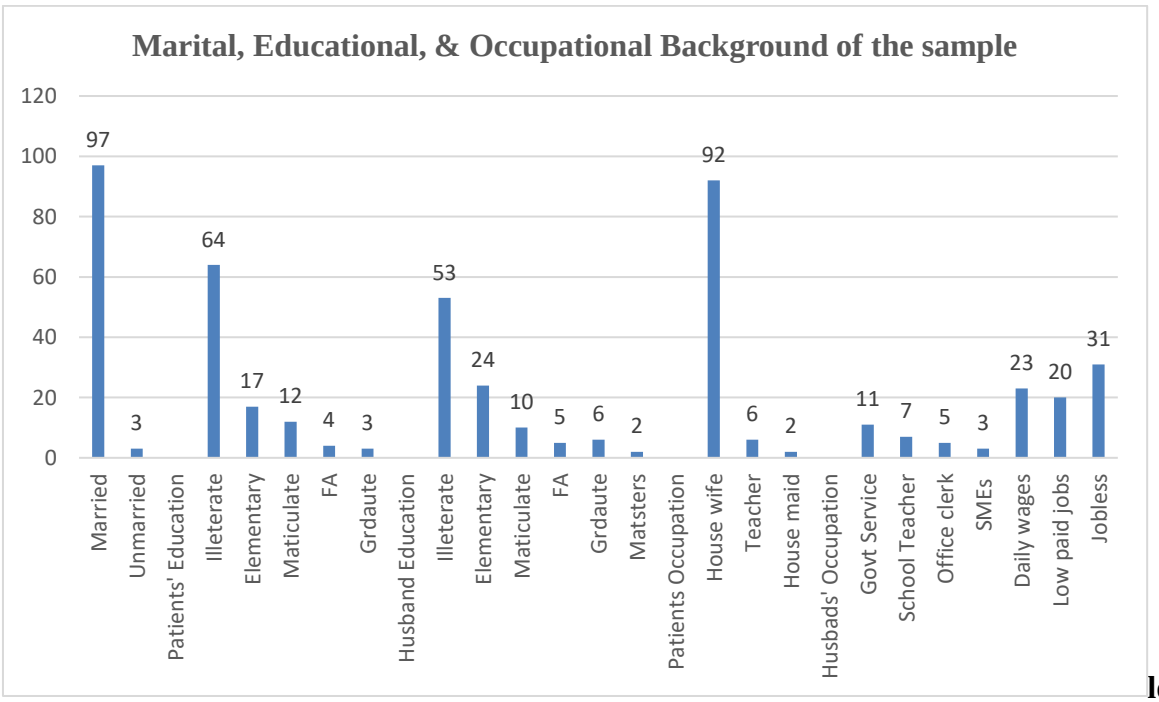

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Figure 2: Marital, Educational and Occupational Background

3.3: Gender Wise Distribution, Family History & Stone Prevalence

The gender wise distribution (Figure 3) showed 95.4% of the patients were females with a 55.2% family history of gall stones (siblings or near relatives). The size and number of stones being diagnosed revealed a varied pattern with multiple stones being more common. The sizes of the stones were directly proportionate to the number of stones being diagnosed. The larger stone size (6.3cm, 2.2 cm) were usually one or one large and few smaller aggregations while the smaller stones of varying measurements (mm) were multiple and vary in numbers being diagnosed. Female gender alone has been shown to be a single strong predictor of gall stones mainly attributed to the increased influence of female sex hormones and increased risk in fertile women who have experienced multiple pregnancies as compared to non-pregnant due to the changes in bile composition and gallbladder stasis [25, 26]. The genetic heritability of symptomatic gallstones is also shown to be a risk of gall stones in the younger population [27].

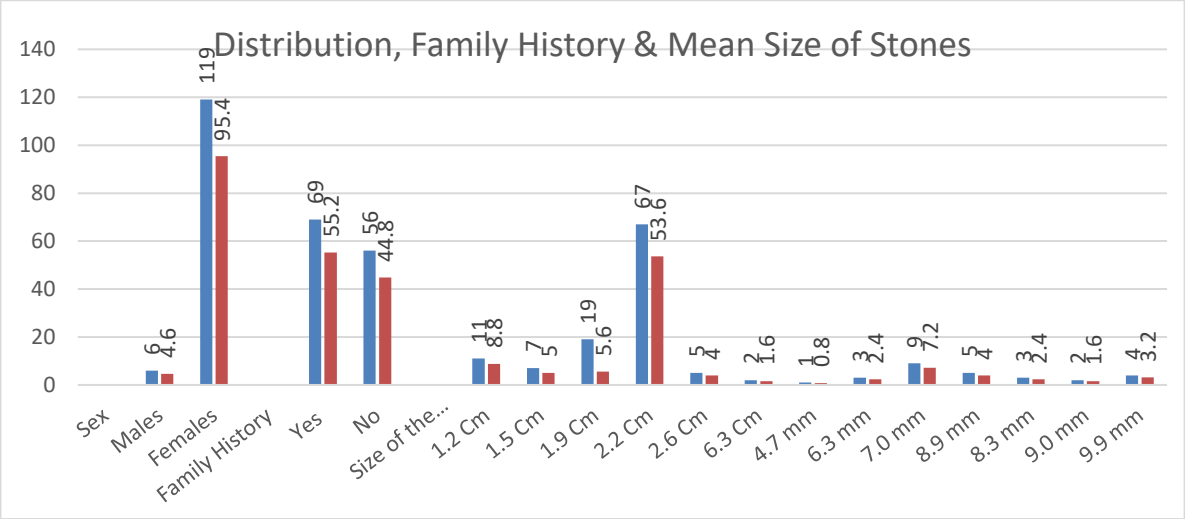

Figure 3: Gender wise distribution, family history& Mean Stone sizes

3.4: Clinical Data of Malnutrition & Symptomatic Cholelithiasis

The clinical signs of malnutrition (Figure 4) indicated majority of the females were having symptoms of iron and Vitamin B complex deficiencies. The most common being paler nails and koilonychia (52%), periorbital dark circles (80%), dry and sparse hair (67%), angular cheilitis (10%), paler complexion (52%). At a public health level, the findings of the current study suggest that iron deficiency and deficiency of other micronutrients may predispose the population subgroups at risks of developing gallstones as suggested by other such studies [28-30].

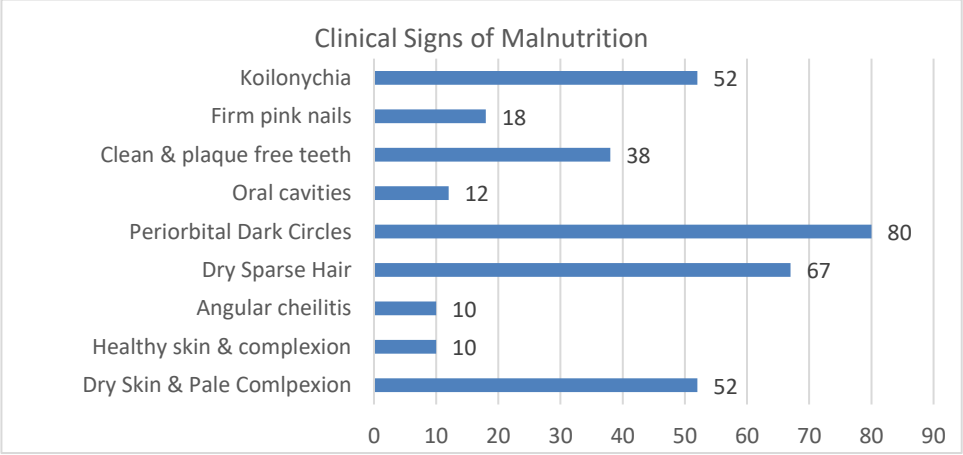

Figure 4: Percent Clinical Symptoms of Malnutrition

3.4: Gastrointestinal and Cholelithiasis Related Symptoms

The percent cholelithiasis related GIT symptoms are given in Figure 5. Results indicated that only 12% of the patients had white to pale yellow stools (an indication of fat malabsorption). Majority of the patients complained about upper right quadrant pain (85%), central abdominal pain (90%), right shoulder and back pain (78%), constipation (47%), indigestion (74%), nausea and vomiting after meal (47%), and gas and bloating (95%). often asymptomatic the gallbladder stones are either diagnosed accidently or through a referral by the medical emergency with the usual gastrointestinal symptoms as reported by the patients in the current study [32].

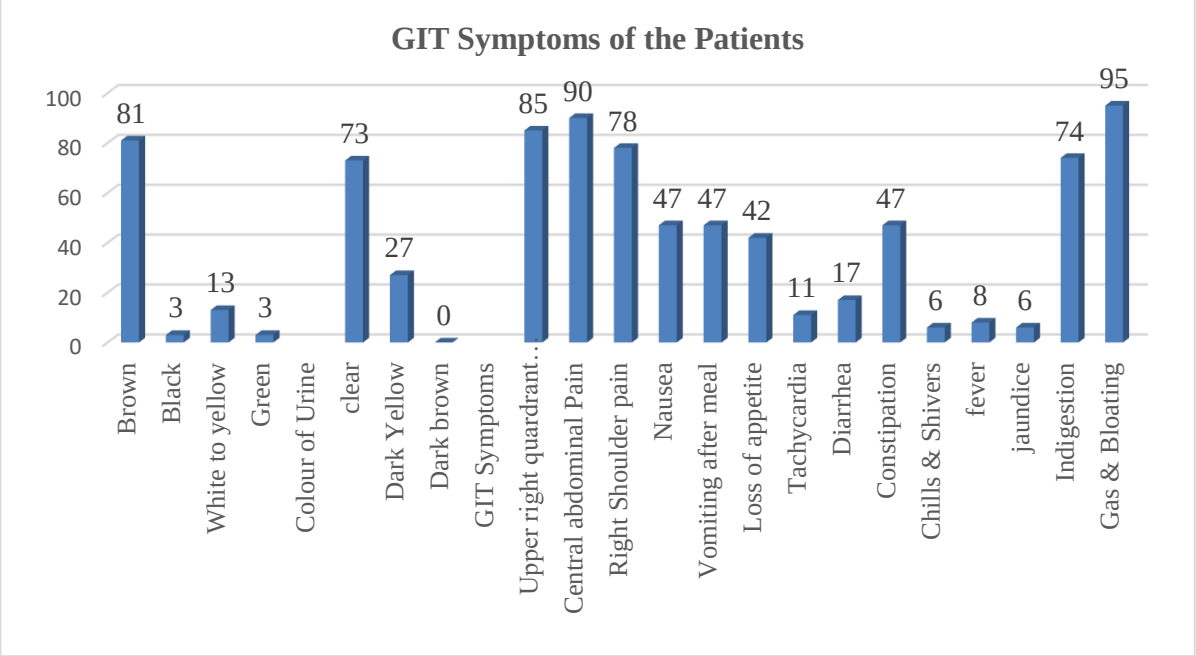

Figure 5: Percent GIT related Symptoms of Cholelithiasis within the sample

3.5: Anthropometric Data of the Sample

The anthropometric measurements (Table 1 & Figure 6) showed mean age of 43.2± 21.39 with a relatively shorter mean heights (5.42±0.16) as compared to the reference heights for Pakistani females, mean weight (69.93±14.93) larger mean waist circumferences (41.49±11.32), higher BMI (26.73±9.85), waist to hip ratios (0.99 ± 8.65) indicated a stronger tendency towards overweight and obesity trends among the patients though these differences were significant at P≤0.05 within the given sample based on age as factor. Similarly, the mean percent body fat and mean visceral fat (36.25 ± 11.72 & 10.19 ± 19.26) indicated higher adiposity in patients of the current study. Based on BMI the data indicated 39.2 % obese and 38.4% overweight patients while only 20% patients fell in the normal range of BMI. From the previous studies adiposity has been consistently associated with gallstone disease risk. Anthropometric measures, Body mass index (BMI), waist circumference, waist-to-hip ratio all have been shown to independently contribute to risk of developing gall stones [33-35].

Table 1: Anthropometric Data of the Sample

PARAMETERS	MEAN±SD	Inter Quartile Range	P -LEVEL	Reference values
Age (Year)	43.2±21.39	22 – 60	0.00	---------
Height (feet and inches)	5.42±0.16	4.11 - 5.6	0.010	159 cm
Weight (Kg)	69.93±14.93	57.6 – 91.5	0.052	59 kg
Waist Circumference(inches)	41.49±11.32	29.6 – 47.2	0.028	31.5 WHO

BMI	26.73±9.85	21.3 – 33.3	0.05	18.5-24.9
MUAC (inches)	14.02±1.72	21 .9 – 26.7	0.001	--------
Waist to Hip Ratio	0.99 ± 8.65	0.80 – 1.47	0.03	above 0.85
Percent Body Fat	36.25 ± 11.72	20.0 - 53.00	0.007	25-31
Visceral fat%	10.19 ± 19.26	6.0 - 19.00	0.04	<10

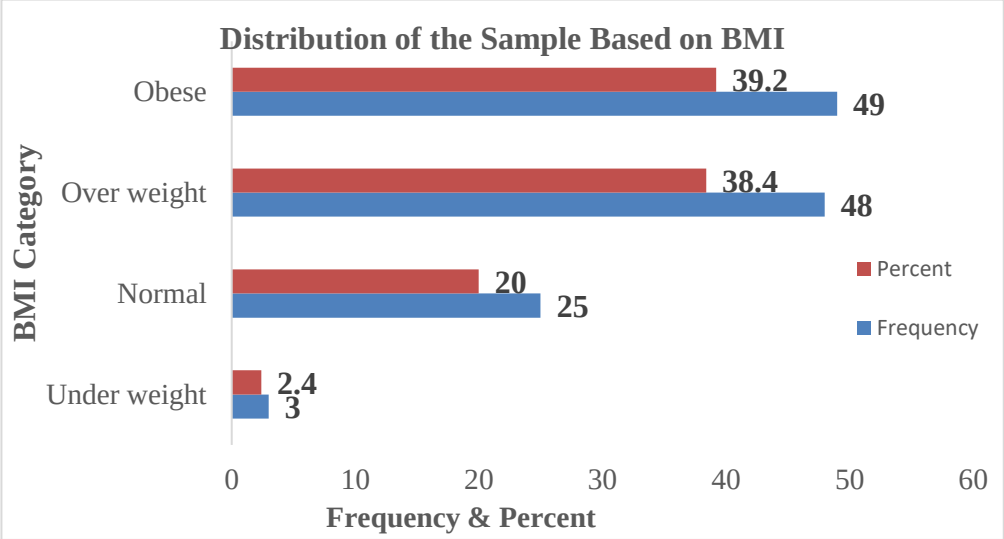

Figure 6: Sample Distribution Based on BMI

3.6: Biochemical Profiles of the Sample

The biochemical data of the patients is given in Table 2. Almost all the parameters of the liver function were within the normal ranges showing gallstone disease being the major reason of patients' attending the gastroenterology departments and their referrals to the imaging scans labs for diagnosis. The mean number of confirmed stones from the ultrasonographic reports being 4.23±18.52 with a significant different within the sample indicated multiple stones being more common within the current study. The prevalence of multiple stones in the current study are strong agreement with another such study at Karachi, Pakistan [36].

Table 2: Hepatic Profiles & Number of Stones of the Patients

PARAMETERS	MEAN±SD	P Level	Normal ranges
Bilirubin	0.71±0.36	0.06	0.1-1.2mg/dl
ALT	36.8±19.13	0.008	7-55U/L
ALP	97.2±58.7	0.09	45-115U/L
No. of gallstones	4.23±18.52	0.003	----------

3.7: Dietary Data

The food frequency (Table 3) indicated wheat being the staple food taken in the form of breads in one form or another. The striking feature was the 85% daily intake of the local flattened bread fried in hydrogenated fat (paratha) which might have contributed to larger caloric intakes and the presence of saturated fats in itself might have posed a risk factor. The percent weekly intake of rice, kitchri (rice cooked with lentils), beans and lentils on most days of the week were good (19.0, 40.0, 37.0, 21.0, 41.3, 23.5, 54.2, 37.2 respectively). The daily intake of milk in the form chai/milk tea was very high (99.5) with 58.0 % of the respondents consuming sugar added chai 2-3 times a day. A surprisingly 24% of the sample consumed milk cream on daily basis usually as a part of breakfast.

The percent intake of beef and minced beef once a week was most common (64.0, 53.0) with 13.0% of the respondents (mainly the male patients) consumed chapli kababs (the local delicacy of beef pattie fried in tallow or ghee). The percent intake of root/tubers vegetables intakes showed the highest consumption on many days of the week (78.0, 74.5, 68.5 respectively) followed green colored vegetables (58.0%) and green leafy vegetables (46.0% & 24.0%). The intake of seasonal fruits was varied across the sample though the intake of mangoes & watermelon on daily basis (40.0, 23.0) was mostly consumed by the male respondents. While the rest of the patients had a chance to get seasonal fruits once a week that too among a smaller number of participants. The per week consumption also identified the risk factor of higher consumption of fruits with high glycemic index carbohydrates and fructose content from the long list of locally available fruits in the market. The once-a-week consumption of biscuits (58.0), and 2-3 times intake of Pakora (fried chickpea flour-based snacks) and samosa (fried potato filled pattie) was higher (33.0% & 31.0% respectively). Hydrogenated fat (ghee) was the major fat in cooking (96.0%) while white sugar was the major sweetener (mainly in tea) in 97.0 % patients. The dietary intake patterns that are identified in the current study are in strong agreement with the findings of other such studies from Pakistan [37].

Table 3: Food frequency (% per day, week, and month) of the Different Food Groups

FOOD GROUP	PERCENT FREQUENCY							
	INTAKE/DAY			INTAKE/WEEK			INTAKE/MONTH	
	1 per day	**2-3 per day**	**4-6 per day**	**1 per week**	**2-3 per week**	**4-6 per week**	**1-2 per month**	**Rarely or never**
CEREALS AND GRAINS								
White bread	0	0	0	0	4.0	0	8.0	88.0
Leavened Wheat Roti	96.0	40.0	0	0	0	0	0	0
Chapatti	1.0	55.0	26.0	4.0	6.0	4.0	1.0	3.0
Paratha	85.0	7.0	0	0	2.0	4.0	0	2.0
Tandoori roti	3.0	15.0	1.0	8.0	33.0	14.0	17.0	9.0
Rice	0	0	0	19.0	40.0	4.0	5.0	86.0
Kitchri	0	0	0	37.0	21.0	0	19.0	23.0
Beans	3.0	0	0	41.3	23.5	31.9	0	0
Cereals/lentils	3.3	3.0	0	5.3	54.2	37.2	0	0
Sandwich	0	0	0	1.0	0	0	16.0	83.0
MILK AND MILK PRODUCTS								
Buffalo/Cow milk (Tea)	99.5	58.0	4.0	42.0	18.0	0	0	13.0
Plain yoghurt	16.0	0	0	28.0	21.0	14.0	17.0	4.0
Cream	24.0	0	0	3.0	16.0	17.0	12.0	8.0
Milk based Desserts	0	0	0	9.0	0	0	73.0	17.0
MEAT AND MEAT PRODCUTS								
Beef	0	0	0	64.0	21.0	2.0	5.0	8.0
Minced beef	0	0	0	53.0	8.0	0	15.0	24.0
Chicken	0	0	0	10.0	0	0	4.0	86.0
Chapli kabab	0	0	0	13.0	4.0	0	64.0	19.0
VEGETABLES								
Green vegetables	0	0	0	58.0	2.0	0	16.0	4.0
Leafy vegetables	0	0	0	46.0	24.0	7.0	0	0
Flower vegetables	0	0	0	16.0	12.0	0	25.0	0
Root Vegetables	0	0	0	78.0	74.5	68.5	0	0
Cucumber (salad)	4.0	0	0	61.0	17.0	8.0	9.0	1.0
Carrot (Salad)	0	0	0	14.0	2.0	0	13.0	1.0
Onions/Tomatoes (cooking)	74.0	11.0	3.0	6.0	0	0	0	0
White colored Vegetables	0	0	0	13.0	1.0	1.0	22.0	63.0
Purple Colored Vegetables	0	0	0	27.0	1.0	0	13.0	9.0
Vegetables in season	0	0	0	85.0	8.0	0	4.0	3.0
Gourds	0	0	0	23.0	7.0	0	36.0	34.0
FRUITS								
Fresh Fruit Salad	0	0	0	0	0	0	24.0	76.0
Apples	0	0	0	18.0	0	0	71.0	11.0
Bananas	4.0	1.0	0	21.0	4.0	0	50.0	20.0
Grapes	0	7.0	0	8.0	5.0	3.0	55.0	22.0

Mango	40.0	10.0	0	13.0	14.0	10.0	10.0	3.0
Watermelon	23.0	1.0	0	34.0	11.0	10.0	14.0	7.0
Melon	0	2.0	0	31.0	5.0	3.0	26.0	31.0
DRINKS								
Pure juice	0	0	0	1.0	0	0	13.0	86.0
Black tea	95.5	58.0	4.0	0	0	0	0	4.0
Green tea	15.0	2.0	0	0	0	0	33.0	60.0
Soft drinks	0	0	0	8.0	2.0	2.0	44.0	44.0
BAKERY, CONFECTIONARY, FRIED/PROCESSED ITEMS								
Plain biscuits	2.0	2.0	0	58.0	5.0	5.0	22.0	8.0
Plain cake	0	0	0	7.0	0	0	30.0	63.0
Gajar ka halwa	0	0	0	0	0	15.0	0	85.0
Sweets/ halwas	0	0	0	2.0	2.0	0	33.0	63.0
Pakora	0	0	0	27.0	33.0	4.0	18.0	18.0
Samosa	0	0	0	28.0	31.0	5.0	17.0	19.0
Chana chat	0	0	0	32.0	4.0	0	31.0	33.0
French fries	0	0	0	17.0	5.0	0	36.0	42.0
FATS, OILS & SUGARS								
Vegetable oil	2.0	2.0	2.0	0	0	0	1.0	93.0
Hydrogenated fat (Ghee)	96.0	96.0	96.0	0	0	0	1.0	0
Desi ghee	2.0	0	0	0	0	0	1.0	97.0
White Sugar	97	79.0	4.0	0	0	0	0	0
Jaggery	03.0	06.0	4.0	39.0	0	0	12.0	36.0

3.8: Macronutrient Intake of the Sample

Results of the macronutrients intakes as means of the three days dietary recalls (Table 4) showed higher consumption of total energy, carbohydrates, fats and sugars from the diets of the studied sample. The percent contribution of the energy (+121.39%) was much higher than the recommended daily intakes (RDAs) for the Pakistani adults of this age group. The overall intake of dietary protein was low (-67.35%) though the interquartile range showed that some patients consumed up to 56.42± 21.25g protein (the major source being the day was of beef intake by some and beans/lentils intake in those three days). The overall carbohydrate intake was much higher (+166.69%) throughout the recall period and almost all the patients had wheat or rice one to three times a day. The total fat intake also showed similar pattern (+159.83) than the recommended 30% of the total calories/day. Two major reasons that were identified in the current study was the overall higher use of saturated fats in cooking (being estimated indirectly through monthly purchase of ghee) and the daily intake of paratha (flattened fried wheat bread) being the major contributor to the poor stat). The major sources of sugars of carbohydrate and fat intakes. The intake of total sugars (means of three days) was also quite higher (114.86%). The major source of sugars in the diets were found to be sugar or jaggery sweetened tea (chai) many times a day and higher intakes of fructose from fruits among some patients. The mean fiber intake was quite low (-49.17%). The contributing factor to the low dietary fiber intake was found to be the gross intake of refined wheat flour being staple food, white rice and the root vegetable in the form of potatoes and the absence of salads in the diets of many patients though some patients scored good in fiber intakes due to consumption of fruits. How dietary factors and nutrient composition predispose a person to the formation of gallstones is still unclear, but many studies have shown that dietary risk factors such as increased cholesterol intake, increased consumption of refined sugars, increased saturated fat intake, tamarind, consumption of high glycaemic index foods, decreased calcium intake, and low dietary fibre intake are risk factors for gall stones. Many studies showed that fibre, especially bran, can reduce the incidence of gallstones [38, 39].

Table 4: Mean Macro Nutrient Intake of the Sample

	Nutrients	**Inter quartile Range**	**Mean ±SD**	**RDA***	**% Contribution in the RDA**
1	Energy (Kcal)	1127.0- 4596.0	2964.29 ± 99.29	2350	+121.39
2	Protein (gm)	16.00 – 56.42	38.62 ± 5.58	46	-67.35
3	Fats (30% Kcal)	60.00 – 199.72	101.39 ± 28.25	65	+151.83

4	Carbohydrates (60% of RDA)	269 – 436.47	336.94 ± 16.58	225	+166.69
5	Sugars/Jaggery	21.75 – 42.20	37.23 ± 13.11	30	+114.86
6	Fiber	7.61 – 26.25	12.3 ± 16.84	18-25	-49.17

3.9: Physical Activity Patterns of the Sample

The physical activity patterns and estimated sitting hours of the study sample are given in figure 7. As evident majority of the patients fell in the category of inactive (44.8%) with patients being involve in little or no activity (did not meet the criteria of other two categories. Similarly, most of the patients were minimally active (46.2%) with the respondents being involved in either up to 20 minutes of vigorous activity on three days or moderate intensity activity or walk of at least 30 minutes up to five days of the week or a combination of both on at least six days of the week. In the current study only 7.5% were HEPA (Health Enhancing Physical Activities) active with the respondents being involved in vigorous strength activities for minimum three days or a combination of vigorous and moderate intensity activities and walking on many days of the week. Metabolic equivalents also showed almost the similar patterns with the highest percent of patients lied in the 330 – 600 METs/week (47.2%) and only 9.3% fell in the 3000-4500 METs min /week. The major contribution to the inactivity were longer sitting hours by 59.6% of the sample attributed mainly the females were house wives and restricted to house chores and males' patients mainly comprised of office workers or school teachers. Physical activity alone has been shown to be a strongest risk factor for the etiology of gall stones as reported by many such studies [40, 41].

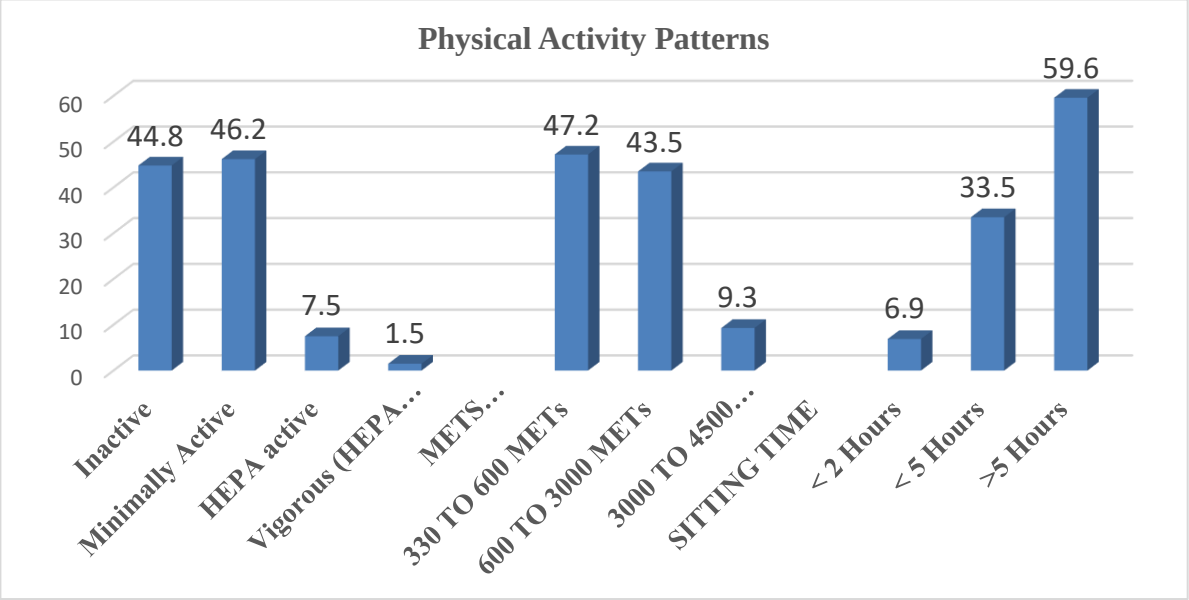

Figure 7: Physical activity Patterns of the Sample

3.10: Association of the Anthropometric Measures, Adiposity, and Macronutrients

The association of anthropometric measurements with macronutrients, physical activity, menopause and parity (Table 5) have shown strong positive correlations among the many variables. Increasing age has shown to have significant positive association with body weight (.354), BMI (.357), MUAC (.226), triceps skinfold thickness (.167), and percent body fat composition (.341, .369). The correlation among all the anthropometric components have shown significantly higher positive correlations with each other indicating an obvious physiological response of the body to the increasing body weight. The correlation co efficient of macronutrient intakes with the anthropometric measures indicated positive relationships of total energy intake, carbohydrates, sugars, and fats with body weight, BMI, Waist to hip ratio, percent total body fat, and percent visceral fat. These significant

positive correlations confirm the mean macronutrient intakes (Table 4) and BMI status of the patients. The non- significant association of age with adiposity among these patients has recently been reported to be independent of aging in many studies suggesting the importance of weight management as an effective way of reducing the prevalence of gallstones [42-44]. The pathophysiological mechanisms, as suggested, that the risk of gall stones increase with increasing adiposity are multifactorial. The primary risk of excess cholesterol being released by the hepatocytes as major consequence of obesity [45, 46]. As estimated an increase of each kilogram of body weight contribute to 20mg of additional cholesterol production which further saturate the bile and precipitation and formation of stones. Visceral fat that accumulates in the abdomen is state to be more metabolically active and increases the hepatic exposure to unesterified fatty acids and decreases insulin sensitivity. This intra-abdominal fat mass has also shown to be positively associated with gallbladder volume [47, 48]. Dietary lipid has been shown to be the stronger mediators of gall stones' risk specifically the saturated and trans fats intake [49, 50]. T has been shown that women in the peri menopause and in post menopause are at increased risk of gall stones due bile and cholesterol deposits in the gallbladder for longer time especially among sedentary and overweight women. The association of physical activity with the anthropometric components has surprisingly shown an inverse/negative correlation indicating the positive role of physical activity in the prevention of obesity and cholelithiasis. Physical activity has shown multitude of benefits in terms of weight loss, weight management and some studies have shown the protective effects of physical activity against the formation of gall bladder aggregations [51-56].

Table 5: Correlation Coefficients of the Risk Factors of Cholelithiasis

PARAMETERS	Age	Weight	BMI	MUAC	Skinfold Thickness	WHR	%Body Fat	%Visceral Fats
Age		.354**	.357**	.226**	.167*	.302**	.341**	.369**
Weight			.910**	.167*	.545**	.366**	.651**	.642**
BMI				.093	.476**	.399**	.651**	.722**
MUAC					.180*	-.058	.211*	.093
Skin Fold Thickness						.200*	.512**	.243**
WHR							.265**	.332**
%Body Fat								.480**
%Visceral Fats								
Energy (calories)	.035	.762**	.514**	.173**	0.131	-.711**	.912**	.812**
Dietary Sugars	.402	-.189**	-.167**	.298**	.079	-.241**	-.307**	.601**
Carbohydrates	.015	.742	.934	.592	.124	.579	.578	.926
Dietary Fats	.163	.632**	.517**	.142*	.347*	.438**	.736**	.581**
Physical Activity	-.329**	-.852**	-.42**	-.244*	-.144*	-.517**	-.774**	-.802**
Menopause	.782**	-.352**	-.305**	-.158*	-.103	-.361**	-.269**	-.316**
Parity	0.107	0.198**	0.073**	0.053	0.040	0156*	-0.145**	0.106**

*. Correlation is significant at the 0.01 level

*. Correlation is significant at the 0.05 level

BMI= Body Mass Index, MUAC= Mid Upper Arm Circumference, WTHR= Waist to Hip Ratio

Delimitations

The study was conducted in two government teaching hospitals and some Ultrasonography clinics in district Peshawar. In order to determine the association of gall stones with genetics, dietary diversity and other epidemiological factors a broad range study is to be carried out at KPK in order to confirm the findings of the current study (future prospects of the author).

Conclusion

The present study led to the conclusion that gallstone disease is more prevalent in married females mostly illiterate housewives. Multiparity and large family size, aging, overweight & obesity specifically the higher adiposity even in normal weight were found to have strong association with

the incidence of gallstone disease. The physical signs and symptoms of the patients are indicative of the presence of micronutrient deficiencies mainly attributed to poor dietary choices. The biochemical ranges of bilirubin, ALT and ALP levels were also found to be normal indicating that the cholelithiasis may be have remained asymptomatic among these patients without other hepatic health related complication. The study also concludes that poor dietary intake patterns, higher total energy, carbohydrates, fats (hydrogenated fat), sugars and lower consumption of dietary fiber and less physical activity may be the strongest predictors of the development of gallstone disease. This necessitate nutrition education to be an integral part of educational and health sectors.

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