Pakistan J. Zool., vol. 38(1), pp. 49-54, 2006.

Effect of Overweight and Obesity on Liver Function in a Sample From Pakistani Population

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Abstract.- The present study was an attempt to document the number of overweight and obese in a sample of normal individuals and to relate both these two factors with the liver function. The study was prospective and a total of 99 male and female individuals of ages between 20-65 years were included and serum lipids and liver enzymes were evaluated. According to BMI, 28% individuals were normal, while 41% and 31% were overweight and obese, respectively. Obese females had greater BMI than males, while males had greater WHR. Cholesterol levels did not differ significantly from normal but a trend of greater cholesterol levels in males of all groups than the females was noticeable. Significantly greater triglyceride levels were found in overweight and obese males only. Alanine aminotransferase (ALT) and asparte aminotransferase (AST) levels showed significant elevations in obese males while in overweight males they were on the rise. Alkaline phosphatase (ALP) levels elevated significantly in obese females only. Correlation analysis demonstrated that ALT was positively correlated with age, BMI, cholesterol, triglyceride, AST and ALP in both females and males. The study implicates that overweight and obesity significantly affects liver function and may lead to further complications of the liver. Serum ALT best indicates liver dysfunction.

Key words: Obesity, liver enzymes, BMI, total lipids, cholesterol.

INTRODUCTION

Overweight refers to increased body weight in relation to height, when compared to some standard of acceptable or desirable weight. It may be due to an increase in body fat or lean muscle (Sorbi *et al.*, 1999). Obesity can be defined as an extensive amount of body fat, which increases the risk of medical illnesses and premature deaths. Body mass index (BMI), despite its limitations, is the true reflection of visceral body weight and obesity (Gallagher *et al.*, 2000). Waist circumference (WC) gives information about abdominal adipose tissue. Waist hip ratio (WHR) of $\geq$0.90 in men and $\geq$0.85 in women is considered a risk for liver disorder connected with obesity (Farrell, 2003). Resting energy expenditure (REE) is typically greater in obese than in the lean persons (Pinto *et al.*, 1996). Overweight and obesity are potential risk factors for devastating diseases such as hypertension, coronary heart disease, hyperlipidemia, type-II diabetes, insulin resistance, stroke, cancers, sleep disorders and several others. Liver is profoundly affected by obesity where it may be associated with hepato-megaly, increased liver biochemistry values and alterations in liver histology like macrovesicular steatosis, steatohepatitis, fibrosis and cirrhosis (Mokdad *et al.*, 2001). In the last 20 years, the prevalence of obesity has increased markedly in industrialized and non-industrialized countries and is likely to continue to increase. According to an estimate there are now more than 500 million overweight and 250 million obese adults in the world (Bray, 1999). Since obesity is increasing in all age groups in Pakistan too and most people who otherwise appear healthy quite possibly be suffering from overweight and obesity and at the same time are unaware of what troubles they might be getting (Alan and Alam, 2004). The present study was undertaken to estimate the number of individuals that turn up overweight and obese in a small sample of population and whether or not these conditions have affected their liver function.

0030-9923/2006/0001-0049 $ 8.00/0

SUBJECTS AND METHODS

A total of 99 healthy subjects including 58 females and 41 males aged 20-65 were randomly selected for the study. All subjects were from different socio-economic groups. Anthropometrical measurements including age, height, weight, waist and hip circumference were recorded and each individual was questioned about the duration of complaints (if any) specific for overweight and obesity. To remove bias, subjects with known hypertension, diabetes, obesity, alcoholics etc. were excluded from the study. The duration of the study was three months. A written informed consent was obtained from each subject and the procedure pertaining to study was explained to each subject. All procedures for the study were approved by the ethical committee of Ministry of Health and Pakistan Medical and Dental Council.

Body mass index (Kg/m^2), waist circumference (cm) and waist-hip ratio were calculated according to standard procedures. BMI $\geq$ 24.9kg/m^2 was considered cut off value for overweight and subjects were considered obese if they had BMI $\geq$ 30Kg/m^2. For waist circumference, WC $\geq$ 97 cm and 85 cm were the cut off values in case of men and women respectively. Similarly waist-hip ratio (WHR) of $\geq$ 0.90 and 0.85 for men and women respectively were considered as cut off values. Serum samples were collected after 12 hrs of fasting. Serum triglycerides (TG) and cholesterol levels were determined on a multichemical fully automated chemistry analyzer by kinetic method using commercially available kits from Linear Chemicals (Spain). Absorbance was recorded and values were calculated as: $A_{sample/}\ A_{standard} \times$ standard concentration=mg/dl cholesterol or triglycerides. Liver function tests were carried out on the same instrument using commercially available kits from Pioneer Diagnostics (USA). Procedure and standard values were as described in the methods of the kits used. For ALT (SGPT) and AST (SGOT), the average absorbance per minute was determined as: ΔA/min × 1746 = GPT or GOT activity at U/Lat 340nm. For ALP, the average absorbance per minute was determined as: D mA/min × 2713 =ALP activity at U/Lat 405 nm.

Values are expressed as mean ± standard error of mean. Comparison within one group was done using Student's t-test. P<0.05 was considered significant. Comparisons between control, overweight and obese groups were made using one-way ANOVA. A probability p value less than 0.05 was considered significant difference. Correlation analysis was done in order to determine the correlation of ALT with different parameters studied. Multiple regression analysis was performed to find out association of different parameters with overweight and obesity.

RESULTS

Only 28% males and females had their BMI within 18.5-24.9 kg/m^2. Individuals with BMI within 25-29.9 and $\geq$30 kg/m^2 were considered overweight and obese respectively. Among 41% overweight individuals, 52.5% were females and 47.5% were males while among 31% obese individuals, 74.1% were females and 25.8% were males. Thus male to female BMI ratio was 1:1.4 and of this, maximum were females. Mean waist circumference in overweight and obese males and females was on significant rise (P<0.05) but waist-hip ratio although slightly elevated in obese groups did not show any significant difference from normal subjects. Cholesterol levels were no different from the normal value in both females and males but triglyceride levels showed significant elevations (P<0.01). However, increase in triglyceride levels was found in overweight and obese males only. Mean ALT levels showed significant increase in obese males only (P<0.01). AST levels for both males and females were within the normal range when compared with standard values. ALP levels were elevated significantly (P<0.05) in overweight and obese male groups only (Table I).

Correlation of ALT was determined to question its dependence on other variables. In overweight females, ALT was positively correlated with age and cholesterol, while TG showed least positive correlation with ALT. AST showed a high positive correlation with ALT while ALP showed least positive correlation. Among obese females, age and BMI were negatively correlated with ALT. On the other hand, cholesterol and TG showed a least positive correlation. By contrast AST and ALP showed a high positive correlation with ALT (Table II).

Among overweight males, ALT was negatively correlated with age and cholesterol, while a least positive correlation in case of BMI and a positive correlation with TG were observed (Table II). Both AST and ALP showed a high positive correlation with ALT in overweight males. In case of obese males, ALT showed a high positive

Table I.- **Age, body mass index, waist circumference, waist-hip ratio, serum lipids and liver enzymes in normal, overweight and obese individuals. Values are expressed as Mean ± SEM.**

Parameters	Normal range	Group I (Normal)		Group II (Overweight)		Group III (Obese)	
		Females (n=14)	Male (n=14)	Females (n=21)	Males (n=19)	Females (n=23)	Males (n=8)
Mean age (yrs)	-	31.64±2.53	38.21 ± 2.03	32.19 ± 2.34	39.79 ± 2.65	38.43 ± 2.50	34.13±3.19
BMI (Kg/m^2)	Female and Male = 18.5-24.9 Kg/m^2	22.60±0.63	21.67 ± 0.56	27.30±0.33 *	27.26±0.32 *	33.89 ± 0.63 *	32.26±0.69 *
WC (cm)	Female ≤ 85 cm, Male ≤ 97 cm	76.76 ± 2.42	83.86 ± 2.60	89.80±.93 *	101.26±1.78*	102.20±2.23*	111.81± 4.23*
WHR	Female≤ 0.85, Male ≤ 0.90,	00.76 ± 0.02	00.85 ± 0.02	00.84±0.02	00.91 ± 0.02	00.86 ± 0.02	00.96 ± 0.02
Cholesterol (mg/dl)	Female and Male ≤ 200 mg/dl	0154 ± 6.38	170.5 ± 6.70	159.14±5.31	186.79±5.90	174.87±7.07	185.13 ±8.01
Triglycerides (mg/dl)	Female and Male ≤ 60-150 mg/dl	97.43 ± 9.52	122.07±12.6	115.38±11.26	240.05±25.07	134.87±13.65	184.88±13.99
ALT (U/L)	Female and Male = 10-35 U/L	18.21 ± 1.12	21.17 ± 1.06	22.57 ± 1.64	34.05 ± 2.82	23.13 ± 2.28	40.88 ± 5.44
AST (U/L)	Female and Male = 5-34 U/L	25.20 ± 1.14	25.79 ± 0.90	26.90 ± 1.66	33.68 ± 2.46	26.17 ±1.77	36.13 ± 6.86
ALP (U/L)	Female=42-98 U/L, Male = 53-128 U/L	81.36 ± 5.56	88.21 ± 8.99	100.19± 6.45	103.26±5.02	121.39±9.94	124.63±29.04

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; TG, triglycerides; WC, waist circumference; WHR, waist-hip ratio. P<0.05 was considered significant.

Table II.- **Pearson's Correlation of ALT with different parameters studied in overweight and obese groups. Values given in the table represent correlation coefficient *r*.**

Groups		Age	BMI	Cholesterol	TG	AST	ALP
Group II	Overweight females	+ 0.54*	+ 0.09	+ 0.47*	+ 0.14	+ 0.89*	+ 0.02
	Overweight males	– 0.40	+ 0.20	– 0.14	+ 0.33	+ 0.68*	+ 0.58*
Group III	Obese females	– 0.04	– 0.28	+ 0.02	+ 0.004	+ 0.76*	+ 0.55*
	Obese males	+ 0.64*	+ 0.73*	+ 0.22	– 0.29	+ 0.93*	– 0.46

*Represents high positive correlation with ALT, P<0.05 was considered significant.

Table III.- **Multiple regression analysis of different variables and their association with overweight and obesity**

Groups / Sex	Cholesterol		TG		ALT		AST		ALP	
	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males
Overweight	0.57	0.58	0.17	0.87	0.37	0.80	0.31	0.54	0.79	0.03*
Obese	0.82	0.097	0.12	0.03*	0.88	0.07	0.75	0.13	0.27	0.33

*represents high association. Figures in the table represent P values. P<0.05 was considered significant correlation with age and BMI, while a least positive correlation was observed with cholesterol. Serum TG was negatively correlated with ALT. A high positive correlation of ALT occurred with AST while a negative correlation occurred with ALP.

Multiple regression analysis of different parameters including cholesterol, TG, ALT, AST and ALP was done in order to assess the association of these profiles with overweight and obesity. The analysis was performed for both male and female groups. $P<0.05$ was considered significant association of these variables with overweight and obesity. The analysis showed that only among obese males TG was significantly associated with obesity while overweight males showed significant association with ALP. Among females no such relationship was observed (Table III).

DISCUSSION

A considerable finding of the present study is significantly greater incidence of overweight and obese females. A similar consistency for high prevalence of obesity has been reported in many ethnic minority women, such as African American, Mexican American, Native American, Pacific Islander American, Puerto Rican, and Cuban American women. In the United Kingdom and Europe also, approximately 15% of men and 20% of women are obese (Kopelman, 2000).

Presently, the values of waist circumference and WHR are significantly high in overweight and obese males that perceptibly points toward central or abdominal obesity. This reflects visceral rather than subcutaneous distribution of adipose tissue and is the metabolic factor that correlates best with steatosis and non-alcoholic steatohepatitis (Freedland, 2004).

Abnormal lipid profile is the first clue as regards obesity (Guzzaloni *et al*., 2000). Intriguingly the serum cholesterol levels of overweight and obese groups of both genders were normal indicating that in all probability it does not indicate obesity. This appears similar to a study carried out by Nimer *et al.* (2000) that serum TG in overweight and obese males implicates hyperlipidemia. Hyperlipidemia is a known risk factor for fatty infiltration of the liver, a condition that can progress to cirrhosis and liver failure (Unger, 2003). As a consequence of this close interaction obesity can cause abnormal liver function by increasing triglycerides in the body. There are evidences that fatty liver, the most common hepatocellular change found in liver biopsies in humans, can play a role in the pathogenesis of chronic liver disease (Lee, 1989; Matteoni *et al*., 1999). Gender wise analysis for cholesterol showed that a high percentage of male subjects were overweight and obese. The percentage of subjects with raised cholesterol was significantly greater in overweight and obese males as compared to the overweight and obese females.

Abnormal liver function tests (LFTs) are commonly taken as the first line of indication of liver diseases. Normal or slightly abnormal LFTs do not rule out numerous liver diseases even advanced cirrhosis (Jessic *et al*., 2001). The liver function tests implies standard test for measurement of synthetic liver function (serum albumins), excretory function (bilirubin) and inflammatory activity of hepatocytes (ALP) (Morgan *et al*., 1991). Presently, among overweight and obese females mean ALT value did not show any significant change from normal, whereas in overweight and obese males it was significantly high. This is parallel to earlier findings that obese individuals may have higher levels of serum transaminases than their lean counterparts (Ravussin *et al*., 1982). Noteworthy is the fact that the most common liver enzyme abnormalities in the study presented by Nimer *et al.* (2000) were elevations in ALT (47%) and Gamma glutamyl transferase (γ-GT) (45%) values in hyperlipidemic patients. Greatly increased ALT values in obese males may indicate fatty liver but the gold standard, however, is a liver biopsy to show the typical histological features of NAFLD, which are almost identical to those of alcohol-induced liver damage and can range from mild steatosis to cirrhosis (Kichian *et al*., 2003).

AST was slightly raised in obese males. In females ALT and AST remained normal and well below the levels encountered in males. ALP levels increased significantly in females.

Mean ALT values in overweight and obese males remained greater than the mean AST values in the same groups. Although the ALT levels are higher than AST levels in most instances of NASH (Pinto *et al*., 1996), the AST level may occasionally be higher than the ALT level, especially in the presence of cirrhosis (Bacon *et al*., 1994).

ALP levels are measured routinely in cholestasis, intra hepatic and extra hepatic liver diseases, hyperparathyroidism and hyperthyroidism. It has been postulated that in mild hepato-cellular injury; when the hepatocyte but not the mitochondrial membrane is damaged, cytoplasmic AST, ALT are released into the serum. With more severe hepatocellular injury, mitochondrial membrane damage may result in the release of mitochondrial AST, elevating AST or ALT ratio (Bakerman, 1984). The relationship between body size and osteoarthritis is stronger in women than in men and even small increase in body weight can cause osteoarthritis in women. Thus high female frequency for elevated ALP may indicate high female prevalence for osteoarthritis although conformation is required to show elevated ALP levels among osteoarthritis patients.

The given study was an attempt to find the number of subjects with elevated liver enzymes that were not carried out in previous studies except for ALT and to a lesser extent for AST. Hoy *et al*. (1994) reported that ALT and AST are the most commonly elevated liver enzymes but they usually do not exceed twice the upper limit of normal. Enzyme levels often do not correlate with the severity of histological abnormalities (Matteoni *et al*., 1999). It differs from alcoholic hepatitis in which the ALT activity is higher than AST, except in patients with cirrhosis (Bacon *et al*., 1994; Sheth *et al*., 1997; Nimer *et al*., 2000).

Another important finding of the present study was that the AST/ALT in obese male group was $\leq$1 again pointing towards the increased risk of NASH in obese males. In contrast to patients who have alcohol-induced steatohepatitis, the AST: ALT ratio is usually less than 1 in patients having NAFLD (Klein *et al*., 2002). ALT shows positive correlation with increasing age, BMI, cholesterol and AST in both males and females implicating this to be the diagnostic test for obesity and liver dysfunction.

In conclusion, the present analysis suggests that males are at a greater risk of developing NALD as indicated by raised triglyceride, ALT and AST values. Since ALP values were significantly greater in females, they are most likely to develop arthritis as compared to their male counterparts. Excepting increased BMI and WC in overweight and obese females the rest of the parameters did not show any abnormality. In contrast, overweight and obese males showed significant increase in BMI, WC, WHR, TG, AST and ALP.

ACKNOWLEDGEMENTS

The authors are indebted to the Biological Sciences Department, Quaid-i-Azam University for funding the present research. The authors are grateful to Dr. Shakeel Ahmad, Pathologist, Holy Family Hospital, Rawalpindi, Pakistan for his valuable suggestions.

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(Received 28 September 2005)