VOLUME - 11, ISSUE - 01, JANUARY - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Endocrinology

TO STUDY THE PREVALENCE OF METABOLIC SYNDROME AND LIFESTYLE FACTORS IN SUBFERTILE MALES IN CENTRAL INDIA

Dr. Nayan Gupta*	Resident, Department of Medicine, M.G.M Medical College, Indore, M.P., India. *Corresponding Author
Prof. Dr. Dharmendra Jhavar	Professor, Department of Medicine, M.G.M Medical College, Indore, M.P., India.
Dr. Amit Agarwal	Associate Professor, Department of Medicine, M.G.M Medical College, Indore, M.P., India.
Prof. Dr. V. P. Pandey	Professor and Head, Department of Medicine, M.G.M Medical College, Indore, M.P., India.

ABSTRACT

Background: Male partner constitute the 50% of couple infertility, among which the abnormal semen quality is the most common cause. There are many factors that can affect sperm quality including metabolic syndrome and modifiable lifestyle factors. Previous literatures regarding effects of metabolic syndrome (MetS) and lifestyle factors on semen quality is inconsistent. So, we decided to find the prevalence of metabolic syndrome and life style factors in subfertile low sperm counts males and improvement in semen quality after treating deranged metabolic parameters and lifestyles modification.

Methods: 51 male partners of infertile couple with low normal sperm count included in this study. MetS was defined by the modified NCEP ATP III criteria with the Asian cut-off for waist circumference. Life style modifiable factors are assessed by using a questionnaire. All patients underwent lifestyle modification for a period of 3 months. The association of metabolic syndrome and lifestyle factors with semen analysis was examined and the changes in semen parameters after life style modification was evaluated.

Results: Metabolic syndrome was significantly associated with reduced sperm count and motility. In life style factors, the sperm count with physical activity grades was found to be statistically significant (P=0.002). Sperm motility was negatively associated with stress level, depression level, smoking grades and Homocysteine level. After 3 months of life style modifications, there was significant increase in sperm count and sperm motility.

Conclusions: Acquiring a healthy life style lead to improvement in sperm count and motility and may consequentially reduce the infertility risk in couples. Physician should strongly advise their patients to adopt a healthy life style including daily physical activity and exercise, reduce obesity, to cut out stress and avoid smoking before undergoing medical treatment.

KEYWORDS : Metabolic syndrome, Lifestyle factors, Semen analysis, Homocysteine level

1. INTRODUCTION

According to the World Health Organization (WHO), infertility had an incidence of 8~12% in childbearing couples worldwide, among which 50% of cases are attributable to the male partner.[1] If the semen parameters are not within the normal range, the male may be regarded as Subfertile. Among the causes, the most common is abnormal semen quality which is found in over 90 percent of cases.[2] A semen analysis called abnormal if the sperm count or sperm motility do not meet medical standards. There are many factors that can affect one's sperm count and motility including mainly metabolic syndrome and modifiable lifestyle factors. Metabolic syndrome (MetS) has been defined as a clustering of metabolic disorders characterized by abdominal obesity, dyslipidemia, hypertension and impaired fasting glucose[3]. In recent years, it has been perceived that there is increase in the prevalence of MetS in younger populations and has coincided with a decrease in semen quality among them, possibly through changes in hormone synthesis and sperma togenesis.[4] Modifiable lifestyle factors can also affect the male fertility by altering endocrine profiles, the spermato genesis, and/or the sperm function.[5]That is why we decided to study to find the prevalence of metabolic syndrome and life style factors in subfertile low sperm counts males with normal secondary sexual characters and Improvement in semen quality after treating deranged metabolic parameters and modifying lifestyles.

1. MATERIAL AND METHOD

2.1 Study Population-

The study sample was collected from the male partner of infertile couples who have low sperm count (including oligospermic <15 million and pre-oligospermic 15-50 million) with normal secondary sexual characters and attended general medicine OPD and division of endocrinology in a tertiary care centre for evaluation of infertility. Patients were excluded having erectile dysfunction, suffering from Varicocele and cryptorchidism, had history of long time intake of methotrexate, sulphasalazine, nitrofurantoin, ketoconazole, had history of radiation exposure, suffering from genital infection or STI or any serious/chronic illness or comorbidity, male without secondary sexual characters and Azoospermia males.

2.2 Study Design and Procedure-

We did an observational & Prospective Interventional study. All the patients were explained about the study in detail in their own language including the procedure, risks/benefits, compliance, etc. After their approval to participate in the study, a voluntary written informed consent was obtained from them. They underwent thorough clinical examination including general and systemic examination. On our inhouse centralized fully automated hematology and biochemistry auto analyzer, blood and serum parameters were assessed under supervision and guidance of respective faculty. Special attention was given for assessing the parameters of metabolic syndrome. Life style modifiable factors mainly physical activity and exercise, stress level, depression and smoking were assessed in the study population using a questionnaire, which consist of questions related to physical activity, Perceived Stress Scale (PSS)[6] for evaluating stress level and Patient Health Questionnaire 9 (PHQ-9)[7] for depression.

After obtaining the results of the tests and questionnaire, all

these patients were advised on lifestyle modification as under for a period of 3 months and standard treatment protocol was advised in patients with deranged metabolic parameters[8] and severe depression.

2.3 Lifestyle Modification Protocol-

1. 30-45 minutes of walk daily and exercises to reduce belly
2. Calories intake as per weight reducing or weight maintenance diet
3. Avoid junk food
4. Cut out the stress or find ways to deal with stress
5. Counselling to lowering stress levels
6. Advice to take a proper sleep.
7. Cessation of smoking and alcohol intake.

All these patients were advised to follow-up after 3 months and reassessment of semen analysis as per WHO guidelines was done in our institutional centralized laboratory. Results of the follow-up were compared with the baseline results.

2.4 Definition of Metabolic syndrome-

According to the Harmonized criteria for MetS in 2009 with the Asian cut-off for waist circumference (WC),[9] metabolic syndrome is defined by presence of any three of the following five conditions ; i.e. 1) Increase in the waist circumference (males: ≥90 cm and for females: ≥80 cm for Asians), 2) Hypertriglyceridemia ≥150 mg/dl, 3) Low HDL (Males <40 mg/dl and for females <50 mg/), 4) Raised blood pressure (blood pressure ≥130/85 mmHg or drug treatment for hypertension), and 5) Elevated blood sugar (fasting blood sugar ≥100 mg/dl or drug treatment for diabetes mellitus)

2.5 Questionnaire Assessment-

The Perceived Stress Scale (PSS) is employed, which is a validated abridged version (10 out of 14 items) that measures how often events are perceived as stressful by questioning participants about their experiences over the previous month. Individual PSS scores can range from 0 to 40, with higher values suggesting greater stress perception. Scores ranging from 0-13 would be considered low stress, 14-26 as moderate stress and 27-40 as high perceived stress.[6]

The PHQ-9 is the 9-item depression module, which scores each of the 9 DSM-IV criteria as "0" (not at all) to "3" (nearly every day) and can range from 0 to 27. The PHQ-9 score was divided into the following categories of increasing severity; 0–4, 5–9, 10–14, 15–19, and 20 or greater showing No depression, Mild depression, Moderate depression, Moderately severe depression and Severe depression respectively.[7]

For analysis purpose the smoking group was grouped into three groups, Mild smoking group (≤9 cigarettes/day), Moderate smoking group (10–19 cigarettes/day), and Heavy smoking group (≥20 cigarettes/day).[10]

2.6 Statistical analysis-

The data was initially captured in the customized proforma and then transferred to Microsoft Excel for analysis. For calculating the p values, online statistical software like GraphPad, Epi Info, etc. were used. Comparison of means between two groups was done using Unpaired 't' test and within the group was done using Paired 't' test. Association between two non-parametric variables was done using Pearson Chi-square test. Comparison of means within three groups was done using One-way ANOVA followed by post-hoc Tukey test. A p value of < 0.05 was taken as statistically significant.

2.7 Ethical considerations-

The synopsis was submitted to the Ethics Committee of our institution for review. After obtaining their approval, the study was initiated in our centre. Also prior to the inclusion of any patient into the study, a voluntary written informed consent obtained from patient. All the rights of patients during the study were explained.

2.8 Financial inputs and funding-

The study was conducted at a State Government run hospital, so all the treatments are provided free of cost to the patients. No additional procedure/investigation was done for specific requirement of the study, hence, there was no additional financial burden either on the patient or on institution. Also, the study was not funded by any institution or any pharmaceutical company.

3. RESULTS

3.1 Baseline characteristics of study population-

3.1.1 Metabolic syndrome parameters

43/51 were in the age group 21-30 years and 8/51 were in 31-40 years. In 10/51 (19.6%) sperm count was <15 million and in 41/51 (80.4%) had sperm count between 15-50 million. The mean sperm count was 21.11 ± 12.44 million. Out of 51, 23 was asthenospermic(<40% sperm motility) and mean sperm motility was 43.39 ± 25.83%. 21/51 males were having HDL cholesterol level <40 mg/dL and 30/51 were having HDL cholesterol level > 40 mg/dL. 14/51 (27.5%) males were having triglyceride level <150 mg/dL and 37/51 (72.5%) were having triglycerides level > 150 mg/dL. Metabolic syndrome was present in 30/51 (60.8%) males. After 3 months of lifestyle modification, 23/51 (45.1%) males were having sperm count between 15-50 million and 28/51 (54.9%) males were having sperm count >50 million. The mean sperm count after 3 months of lifestyle modification was 61.09 ± 27.14 million. After 3 months, 6/51 (11.8%) males had sperm motility <40% and 45/51 (88.2%) males had sperm motility > 40%. The mean sperm motility after 3 months of lifestyle modification was 59.57 ± 13.55%. There was a significant improvement in sperm count and sperm motility after 3 months of lifestyle modification (P=0.001).

Table 1- Distribution of study population according to various parameters of metabolic syndrome.

Metabolic syndrome parameters	Range	Number of participants	Percentage (%)
Waist circumference	<90 cm	26	51
	≥90 cm	25	49
HDL level	<40 mg/dl	21	41.2
	≥40 mg/dL	30	58.8
Blood Pressure	<135/85 mm Hg	26	51
	≥ 135/85 mg Hg	25	49
Triglyceride level	<150 mg/dL	14	27.5
	≥ 150 mg/dL	37	72.5
Fasting Plasma Glucose	<100 mg/dL	26	51
	≥ 100 mg/dL	25	49

Table 2- Distribution of study population according to sperm count at enrollment and after 3 months of lifestyle modification

Sperm Count	At Enrollment (Percentage)	After 3 months (Percentage)
<15 million	10 (19.6%)	0
15-50 million	41 (80.4%)	23 (45.1%)
>50 million	0	28 (54.9%)

Table 3- Distribution of study population according to sperm motility at enrollment and after 3 months of lifestyle modification

Sperm Motility	At Enrollment (Percentage)	After 3 months (Percentage)
<40%	23 (45.1%)	6 (11.8%)
≥40%	28 (54.9%)	45 (88.2%)

3.1.2 Life style Factors

On Assessing modifiable lifestyle factors, 20/51 males had sedentary life style, 25/51 had moderate physical activity and only 6/51 had heavy physical activity. Stress level was assessed by perceived stress scale(PSS) which shows Low stress seen in 17/51 (33.3%), moderate stress in 23/51 (45.1%) and high stress in 11/51 (21.6%). Depression is evaluated by PHQ-9, Depression was not present in 15/51 (29.4%), mild depression in 20/51 (39.2%), moderate depression in 10/51 (19.6%), moderate to severe depression in 4/51 (7.8%) and severe depression in 2/51 (3.9%). 28/51 (54.9%) were non-smokers, 9/51 (17.6%) were mild smokers, 8/51 (15.7%) were moderate smokers and 6/51 (11.8%) were heavy smokers.

Table 4- Distribution of study population according to physical activity

Physical activity	Number	Percentage
Sedentary lifestyle	20	39.2
Moderate active	25	49.0
Heavy active	6	11.8
Total study participants	51	100

Table 5- Distribution of study population according to stress level

Stress level	Number	Percentage
Low	17	33.3
Moderate	23	45.1
High	11	21.6
Total study participants	51	100.0

Table 6- Distribution of study population according to depression scale

Depression scale	Number	Percentage
None	15	29.4
Mild	20	39.2
Moderate	10	19.6
Moderate to severe	4	7.8
Severe	2	3.9
Total study participants	51	100.0

Table 7- Distribution of study population according to smoking grade

Smoking Grading	Number	Percentage
Non-smoker	28	54.9
Mild smoker	9	17.6
Moderate smoker	8	15.7
Heavy smoker	6	11.8
Total study participants	51	100.0

3.1.3 Homocysteine

27/51 (52.9%) males had normal homocysteine level, 9/51 (17.6%) males had intermediate homocysteine level and 15/51 (29.4%) males had moderate elevation in homocysteine level.

Table 8- Distribution of study population according to homocysteine level.

Homocysteine level	Number	Percentage
Normal	27	52.9
Intermediate	9	17.6
Moderate elevation	15	29.4
Total study participants	51	100.0

3.2 Associations between Metabolic syndrome and Semen Analysis

At enrollment, the mean sperm count in patients without metabolic syndrome was 32.93 ± 12.41 million and in patients with metabolic syndrome was 18.42 ± 8.66 million. The mean sperm motility in patients without metabolic syndrome was 56.55 ± 26.72% and in patients with metabolic syndrome was 34.90 ± 21.68%. At enrollment, both the mean sperm count and sperm motility was significantly lower in patients with metabolic syndrome compared to patients without metabolic syndrome (P=0.001).

3.3 Associations between Life style factors and Semen Analysis

3.3.1 Physical activity and semen analysis

In sedentary lifestyle, the mean sperm count was 17.15 ± 9.64 million, in moderate physical activity group was 27.30 ± 12.26 million and in heavy physical activity group was 34.00 ± 10.51 million. The comparison of mean sperm count at enrollment in relation to physical activity was found to be statistically significant (P=0.002). While the mean sperm motility also was lowest in sedentary lifestyle and highest in heavy physical activity group but the comparison of mean sperm motility at enrollment in relation to physical activity was found to be statistically not significant (P=0.220), showing a comparable mean sperm motility in relation to physical activity. After 3 months of life style modification, the mean sperm count improved from 17.15 ± 9.64 to 67.85 ± 27.96 million in sedentary life style group and from 27.30 ± 12.26 million to 58.00 ± 26.88 million in moderate physical activity group and the sperm motility improved from 37.50 ± 24.03% to 59.55 ± 12.24% in sedentary life style group and from 44.56 ± 27.58% to 59.44 ± 14.57% in moderate physical activity group. Thus, there was a significant improvement in the sperm count and sperm motility after 3 months of lifestyle modification in sedentary and moderate physical active groups (P=0.001).

3.3.2 Stress level and semen analysis

In low stress group, the mean sperm count was 26.71 ± 11.89 million, in moderate stress group it was 24.50 ± 12.46 million and in high stress group it was 19.27 ± 12.97 million. The comparison of mean sperm count at enrollment in relation to stress was found to be statistically not significant (P=0.303), showing a comparable mean sperm count in relation to stress. In low stress group, the mean sperm motility was 37.50 ± 24.03%, in moderate stress group it was 44.56 ± 27.58% and in high stress group it was 10.27 ± 5.79%. The mean sperm motility was lowest in high stress group and highest in low stress group. The comparison of mean sperm motility at enrollment in relation to stress was found to be statistically significant (P=0.001). After 3 months of life style modification, the mean sperm count was improved from 24.50 ± 12.46 million to 64.57 ± 25.49 million in moderate stress level, from 19.27 ± 12.97 million to 70.82 ± 29.97 million in high stress level group and mean sperm motility improved from 43.65 ± 21.43% to 55.87 ± 13.75% in moderate stress level group and from 10.27 ± 5.79% to 56.36 ± 11.88% in high stress level group. Thus, there was a significant improvement in the sperm count and sperm motility in moderate and high stress level group after 3 months of lifestyle modification (P=0.001).

3.3.3 Depression level and semen analysis

In no depression group, mean sperm count was 28.77 ± 12.34 million, in mild depression group it was 22.65 ± 11.54 million, in moderate depression group was 23.50 ± 13.66 million, in moderate to severe depression group was 16.00 ± 7.79 and in severe depression group it was 23.00 ± 24.04 million. The comparison of mean sperm count at enrollment in relation to depression was found statistically not significant (P=0.401), showing a comparable mean sperm count in relation to depression. While, the mean sperm motility in no depression group was 55.87 ± 19.97 million, in mild depression group it was 47.05 ± 24.87 million, in moderate depression group it was 33.30 ± 28.99 million, in moderate to severe depression group it was 18.25 ± 13.72 and in severe depression group it was 14.00 ± 4.24 million. Mean sperm motility was lowest in severe depression group and highest in no depression group. The comparison of mean sperm motility at enrollment in relation to depression was found statistically significant (P=0.013). After 3 months of lifestyle modification, both the mean sperm count and sperm motility was significantly improved in Mild depression, Moderate depression and Moderate to severe depression group (P<0.05) but not significantly improved in severe depression group (P > 0.05).

3.3.4 Smoking and semen analysis

The mean sperm count in no smoking group was 25.14 ± 12.85 million, in mild smoker group it was 22.33 ± 9.67 million, in moderate smoker group it was 22.81 ± 13.31 million and in heavy smoker group it was 23.67 ± 15.58 million. The comparison of mean sperm count at enrollment in relation to smoking was found statistically not significant (P=0.930), showing only comparable mean sperm count in relation to smoking. While the mean sperm motility in no smoking group was 48.75 ± 24.56 million, in mild smoker group it was 60.11 ± 17.40 million, in moderate smoker group it was 32.88 ± 18.88 million and in heavy smoker group it was 7.33 ± 5.43 million. The sperm motility was lowest in heavy smokers and highest in mild smokers. The comparison of mean sperm motility at enrollment in relation to smoking was found statistically significant (P=0.001). After 3 months of life style modifications, the mean sperm count was improved from 22.81 ± 13.31 million to 52.25 ± 24.97 million in moderate smokers and from 23.67 ± 15.58 million to 64.33 ± 35.83 million in heavy smokers. The mean sperm motility was also improved from 32.88 ± 18.88% to 48.50 ± 11.38% in moderate smokers and from 7.33 ± 5.43% to 52.17 ± 9.02% in heavy smokers. There was a significant improvement in sperm count and sperm motility in moderate and heavy smokers after 3 months of lifestyle modification (P<0.05).

3.4 Associations between Homocysteine level and Semen Analysis

In normal homocysteine level group, the mean sperm count was 23.15 ± 12.17 million, in moderate homocysteine level group it was 26.73 ± 3.15 million and in intermediate homocysteine level group it was 22.61 ± 14.39 million. The comparison of mean sperm count in relation to homocysteine level was found to be statistically not significant (P=0.628).

While the mean sperm motility was 50.22 ± 24.85% in normal homocysteine level group, 41.87 ± 27.31% in moderate homocysteine level group and 25.44 ± 18.24% in heavy homocysteine level group. The mean sperm motility was highest in normal homocysteine level and lowest in intermediate homocysteine level. The comparison of mean sperm motility in relation to homocysteine level was found to be statistically significant (P=0.040).

4. DISCUSSION

4.1 Metabolic syndrome and semen analysis

The prevalence of metabolic syndrome in our study population (60.8%) was higher in comparison of normal adult population in India, which was found to be 30%.[11] **Le et al.**[12] reported a 23.4% prevalence of metabolic syndrome in their study also. The prevalence of metabolic syndrome in our study is higher than that reported by Le. In our study, the mean sperm count and sperm motility was found to be negatively associated with metabolic syndrome. Similar to study done by **Leisegang et al**,[13] reported a lower sperm concentration, a total sperm count, total motility, sperm viability and a higher sperm DNA fragmentation in men with metabolic syndrome. In systematic review and meta-analysis conducted by **Zhao L et al**[14] also found that metabolic syndrome cases had significantly reduced sperm total count, sperm concentration, sperm progressive motility, sperm normal morphology and sperm vitality in comparison to controls. **Chen et al**[15] found that metabolic syndrome was significantly associated with reduced percentage of sperm normal count and morphology. These results are comparable to our study findings. Thus Metabolic Syndrome tended to be a risk factor for male fertility.

The sperm count and motility was statistically significantly improved after 3 months of life style modification compared to the enrollment in the metabolic syndrome patients as well as non-metabolic syndrome patients. Similar result was found in **Håkonsen et al**[16] stated that weight loss in obese men by weight loss programme and life style changes was associated with an increase in total sperm count and semen volume. The group with the maximum weight loss had a significant increase in total sperm count and normal sperm morphology, **Jaffar et al**[17] also found that men who underwent diet counselling and exercise resulting in weight loss, which had significant positive correlation with percentage of progressive sperm motility. **Morgante et al**[18] found that treatment of oligo-terato-asthenozoospermic patients with metabolic syndrome improves semen characteristics.

4.2 Physical activity and semen analysis

In our study, both the sperm count and sperm motility was highest in heavy physical activity and lowest in sedentary lifestyle patients, the comparison of mean sperm count among the three physical activity grades was found to be statistically significant (P=0.002) but comparison of mean sperm motility was found to be statistically not significant (P=0.220). **Jurewicz et al**[19] suggested that leisure time physical activity was significantly associated with increased sperm concentration. Physically active men had more sperm count and higher sperm motility. **Vaamonde et al**[20] also showed physically active subjects had a healthier semen production with improved quality in morphology and total progressive motility. After 3 months of life style modification, there was a significant improvement in sperm count and sperm motility in both sedentary and moderate physical active patients (P<0.05), while heavy physical active patients already have healthy life style so there was no significant improvement (P>0.05). Similarly, **Lalinde-Acevedo et al**[21] also showed that doing regular physical activity improve sperm fertility parameters and such life style can augment the fertility status of men.

4.3 Stress level and semen analysis

In our study, the sperm count among the three stress levels was found to be statistically not significant (P=0.303). While the sperm motility among the three stress levels was found to be statistically significant (P=0.001). Similarly, **Janevic et al**[22] evaluated association between perceived stress and semen quality. Men who experienced stressful life events in the past year had a reduced percentage of motile sperm and reduced morphologically normal sperm in comparison with men who experienced no stressful events but they have a similar sperm concentration. In a systemic review and meta-analyses conducted by **Li et al**[23] found that psychological stress can lower sperm density and sperm progressive motility and increase abnormal sperm. Our study show negative association of stress level only with sperm motility. After 3 months of lifestyle modification including timely counselling to lowering stress levels and to cut out stress factors, the mean sperm count and sperm motility increased significantly in moderate stress level patients (P<0.05) and high stress level patients (P<0.05).

4.4 Depression level and semen analysis

The sperm count was comparable across all the depression grades (P=0.401). But the sperm motility was highest in no depression patients and lowest in severe depression patients and the sperm motility in relation to depression grades was found to be statistically significant (P=0.013). In our study, only sperm motility was negatively associated with depression level unlikely other study where depression is negatively associated with overall semen quality as in **Zou et al**[24] showed a negative association between depression and semen parameters in men mainly semen concentration, total sperm count, and progressive motility. Also in **Yland et al**[25] proposed that history of depression was associated with worse semen quality.

4.5 Smoking and semen analysis

The sperm count was comparable across all the smoking grades (P=0.930), but the sperm motility was highest mild smoker and lowest in heavy smoker. The comparison of sperm motility in relation to smoking status was found to be statistically significant (P=0.001). Similarly also found in **Kovac et al**[26] compared the semen parameters of infertile male smokers with non-smokers and also evaluate comparisons among heavy, moderate, and light smokers. It showed that cigarette smoking can affect male fertility by decreasing the sperm motility and percentage of normal sperm cells. Also in **Lingappa et al**[27] found that Cigarette smoking have a greater detrimental effect on sperm motility in comparison that of sperm count. The results of our study are consistent with a previous researches. After 3 months of life style modifications which include smoking cessation, the mean sperm motility significantly improved in moderate and heavy smokers (P<0.05).

4.5 Homocysteine level and Semen Analysis

In our study, sperm count was significantly not associated with blood homocysteine level but sperm motility was negatively associated with blood homocysteine level. While **Kralikova et al**[28] stated that significant differences or correlations were not found with blood plasma concentrations of homocysteine and semen parameters. **Liu et al**[29] found a negative correlation between serum Homocysteine level with sperm concentration and sperm motility.

5. CONCLUSION

The prevalence of metabolic syndrome was higher in subfertile males and found to be a risk factor for subfertility in males with low sperm count. Thus, metabolic syndrome and modifiable life style factors are associated with semen quality and responsible for detrimental in sperm count and sperm motility that likely lead to infertility. Acquiring a healthy life style lead to improvement in sperm count & sperm motility and may consequentially reduce the infertility risk in couples.

It is concluded that physician should strongly advise their patients to adopt a healthy life style including daily physical activity and exercise, reduce obesity, to cut out stress and avoid smoking before undergoing medical treatment.

Abbreviations- MetS – Metabolic Syndrome, NCEP ATP III- The National Cholesterol Education Program's Adult Treatment Panel III, PHQ-9 - Patient Health Questionnaire-9, PSS- Perceived Stress Scale

DECLARATIONS

Conflict of interest: None

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