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Psychophysiological Status and Life Quality in Individuals with Metabolic Syndrome Living in Central Kazakhstan

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Abstract

BACKGROUND: Morbidity rate of circulatory system diseases (CSD) in Kazakhstan continues to grow and the metabolic syndrome (MetS) contributes significantly to cardiovascular risk development. It was known that MetS altered autonomic nervous system (ANS) by decreasing parasympathetic activity and global heart rate variability (HRV), at the same time, the decrease in sympathetic modulation is unclear. Studies investigated associations between anxiety and MetS disorders are rather controversial. Research findings of the MetS influence on health-related quality of life (HRQoL) were also contradictory. The above-mentioned justifies the necessity of research to clarify and deepen the MetS etiology and pathogenesis, as well as to improve its diagnostics efficiency and treatment.

AIM: The research goals were to study psychophysiological status and HRQoL in individuals with MetS living in Central Kazakhstan.

MATERIALS AND METHODS: Three hundred MetS patients were examined in Karaganda city clinical hospital. Statistical methods and spectral analysis of HRV, simple visual-motor reaction (SVMR), the Spielberger State-Trait Anxiety Inventory, and the Lüscher color test were used. SF-36 questionnaire was used for HRQoL assessment.

RESULTS: General decrease in the activity of both sympathetic and parasympathetic branches of ANS was observed in MetS patients. More than half of the examined MetS patients have had a high level of trait anxiety. Most MetS patients have had a low level of the central nervous system (CNS) functional activity. MetS patients are active both in physical and social spheres. Bodily pain syndrome greatly influences MetS patients' life quality. The patients evaluate their health level as being low.

CONCLUSION: Individuals with MetS living in Central Kazakhstan had decreased activity of ANS, prevalence of inhibition processes in CNS, high level of trait anxiety, and bodily pain syndrome affecting life quality.

Introduction

Morbidity rate of circulatory system diseases (CSD) in Kazakhstan continues to grow and mortality rate of CSD continues to be the main cause of general population mortality among all existing disease classes [1], [2]. In industrial regions of Central Kazakhstan, the development of CSD, among which 75% are arterial hypertension, can be influenced by environmental factors [3]. The metabolic syndrome (MetS) contributes significantly to cardiovascular risk development, with abdominal obesity and hypertension being the leading components [4].

The above-mentioned justifies the necessity of researches to clarify and deepen the etiology and pathogenesis comprehension, as well as to improve diagnostics efficiency and treatment of ecologically caused health issues.

There is strong evidence that obesity leads to an increased sympathetic modulation and a decreased vagal tone, which in turn leads to the lack of autonomic control, characterized by heart rate variability (HRV) reduction. Increased muscle sympathetic nerve activity, changes in renin-angiotensin-aldosterone system and plasma catecholamines are important characteristics of obese individuals [5], [6], [7]. All these factors further contribute to increased blood pressure (BP) 8], [9], [10].

Recently, HRV has become an important instrument for autonomic modulation evaluation. In their study, Koskien *et al*. [11] showed that overall HRV is significantly reduced in adults with MetS. The association of individual components of MetS with HRV differed according to gender. They found that women with MetS had lower vagal activity and that there was a possible increase in sympathetic predominance.

Duanping *et al*. examined the relationship between cardiac autonomic activity level and MetS disorders [12]. In their research, high-frequency (HF) and low-frequency (LF) spectral powers, LF to HF ratio, and the standard deviation (SD) of all normal R-R intervals were used as the conventional indices

of HRV for cardiac autonomic activity measurement. The MetS disorders included hypertension, type 2 diabetes, and dyslipidemia. Findings suggest that MetS disorders adversely affect cardiac autonomic control and that reduced cardiac autonomic control may contribute to the increased risk of subsequent cardiovascular events in individuals with MetS disorders.

Stuckey *et al*. [7] conducted a systematic review on 14 studies published primary researches, which examined associations between HRV, MetS, and its individual risk factors. After the systematic review, it was concluded that the HRV was generally reduced in women with MetS, while results in men were inconsistent. Time and frequency domain of HRV parameters were associated with individual MetS risk factors, though gender differences exist.

It can be concluded that MetS altered autonomic nervous system (ANS) by decreasing parasympathetic activity and global HRV, at the same time, the decrease in sympathetic modulation is unclear.

According to a meta-analysis by Booth *et al*. [13], anxiety among the population remains and has a tendency to spread and grow. Several studies investigated associations between anxiety and MetS disorders; however, findings in this field are rather controversial. Carrol *et al*. [14] report on the positive relationship between generalized anxiety disorder (GAD) and MetS. Similar findings presented by Luppino *et al*. [15], Ribeiro *et al*. [16], and Kahl *et al*. [17] point to the association between anxiety/depression and MetS.

In contrast, Norwegian researchers [18] found no connections between anxiety/depression and MetS. Others reported on exclusively finding depression related to MetS [19], [20].

A number of authors researched MetS influence on health-related quality of life (HRQoL); however, results were contradictory. Iranian researchers [21] showed that MetS was connected to women's low scores in physical functioning (PF), bodily pain, and social functioning domains. Dutch scientists [22] found that both obese men and women with MetS had a higher probability of poor scores in the domains of general health, vitality, social functioning, and role limitations due to emotional problems even after adjusting for body mass index (BMI). According to an earlier study by American scientists [23], this association was eliminated by controlling for BMI. Moreover, they showed that MetS was not associated with lower mental quality of life. On the contrary, Greek researchers [24] found that MetS patients showed significantly lower physical and mental components summary scores than patients without the syndrome.

The research goals were to study psychophysiological status and life quality in individuals with MetS living in Central Kazakhstan.

Materials and Methods

In Kazakhstan, the MetS is prevalent in 25% of the adult population [25]. Based on type I error (α=5%), the required sample size (n) should be equal:

$$n = \frac{t^2 p(100 - p)}{5^2} = 300$$

The study was performed at Karaganda city clinical hospital. Three hundred MetS patients were examined: 192 women and 108 men, aged 18–65 years. According to the authors of diagnostics and management of MetS in the Republic of Kazakhstan, MetS diagnostics criteria should be the same as the European Standards. Studies in Kazakhstan show that the waist circumference (WC) measurement reflects mostly the degree of insulin resistance in patients [25], [26]. By the International Diabetes Federation (IDF) criteria [27] and experts of the Russian Scientific Society of Cardiology on the diagnosis and treatment of MetS [4], MetS was defined as the combination of WC ≥ 80 cm in women and ≥94 cm in men with two and more risk factors (triglycerides ≥1.7 mmol/l, high-density lipoprotein (HDL) cholesterol <1.2 in women, HDL cholesterol < 1.0 mmol/l in men, fasting plasma glucose ≥ 5.6 mmol/l, BP ≥ 130/85 mm Hg, or taking antihypertensive medication). Patients with hyperglycemia had prediabetes and their blood glucose is higher than usual but not so high as to constitute diabetes. Cardiac arrhythmia and cognitive disorder were excluding criteria.

Ethics Committee approved the study. The patients gave informed consent to participate in the research.

Data collection

WC, triglycerides, HDL cholesterol, fasting plasma glucose, and BP measurements were observed. Arterial hypertension (AH) diagnostics were done according to the clinical recommendations [28] and the clinical protocol on AH of Healthcare and Social Development of the Republic of Kazakhstan [29].

Assessment of autonomic regulation of the heart was performed by analyzing HRV using statistical methods and spectral analysis [30].

Central nervous system (CNS) activation level was assessed by simple visual-motor reaction (SVMR) [31].

To determine patients' anxiety level, the Spielberger State-Trait Anxiety Inventory was employed [32].

The patients' psychophysiological state was evaluated by the Lüscher color test [33].

SF-36 questionnaire was used for HRQoL assessment [34].

Statistical analysis

Quantitative data, in the case of the normal distribution, were presented as mean values (M) and standard errors of the mean (m). In the case of non-normal distribution, data were presented in the form of median (Me), lower (Q_{25}), and upper (Q_{75}) quartiles. Qualitative data were presented in the form of a percentage of (p) with a 95% confidence interval (CI). Relationships were assessed by Spearman's rank correlation coefficient. R software was used for calculations.

Results

The clinical study involved 300 patients with MetS, mean age 52.29±8.76 years. Females predominated among the examined patients (63.93±6.15%). Age and gender are presented in Table 1.

Metabolic disorders were most frequent among 40–49 and 50–59 age groups for total subjects (26.33%; CI [21.44–31,70]% and 41.00%; CI [35.38–46.80]%, respectively).

The main components of MetS were obesity (211 patients [70.33%; CI {64.81–75.45}%]) and hypertension (250 patients [83.33% CI {78.62-87.37}%]) with predominating Grade 1 hypertension: (140–159) mmHg systolic and/or (90–99) mmHg diastolic BP (66.67%; CI [61.02–71.98]%). Dyslipidemia was diagnosed in 46% of cases (CI [40.26-51.82]%) and dysglycemia in 27% (CI [22.99-33.45]%).

When describing the condition of MetS patients, it is necessary to evaluate not only carbohydrate and lipid metabolism indicators but also neurohumoral system parameters. To assess the neurohumoral system, HRV analysis was used. This analysis provides information about heart rhythm autonomic regulation and overall status of the ANS [35], [36].

Table 2 data are the integral indicators of HRV in general, reflecting a balance between sympathetic and parasympathetic nervous systems influences.

Presented HRV statistical indicators are generally significantly lower than normative figures. In the study group, SDNN, RMSSD, pNN50% decreased 2, 3, and 4 times, respectively. The average pulse rate was around 80 beats/min. Aforementioned indicators give evidence for autonomic balance shift toward sympathetic nervous system predominance and significant strain in the heart rhythm regulation system.

Spectral analysis components (Table 3) characterize HRV periodic components and can be used for a separate description of both branches of the ANS.

There is a significant decrease in total power (TP) of the cardiointervalogram's spectrum and individual spectral components in the study group, which is evidence of the significant rhythm stabilization. HF component of the spectrum is weakly expressed both in absolute terms HF = (301.83 ± 98.55) ms^2 and percentage HF = (17.56 ± 3.31)% to TP. These fluctuations reflect vagal influences on cardiac rhythm and point to the decreasing activity of the parasympathetic branch in the study group. Low frequency (LF) = (899.19 ± 398.14) ms^2 for the study group, (1170 ± 416) ms^2 for healthy individuals, and very low-frequency components VLF = (330.68 ± 107.68) ms^2 against the normal (1267 ± 400) ms^2 are weakly expressed. Therefore, sympathetic branch activity is also significantly lower in comparison to healthy individuals. Nevertheless, there is a balance shift toward sympathetic branch since LF/HF = 3.77± 0.92.

Thus, no significant peaks were observed, while evaluating the percentage contribution of each spectral component to the total spectral power. LF = 36.12% waves prevail slightly.

The studied sample contained the least number of patients with low trait anxiety (11.11%) (Table 4).

The number of patients with moderate trait anxiety level was two times greater – 27.78%. More than half of the patients (61.11%) had a high level of trait anxiety.

Table 1: Distribution of patients by age and gender

Age group	Total			Male			Female		
years	n	%	95% CI	n	%	95% CI	n	%	95% CI
20-29	15	5.00	2.83-8.11	5	4.63	1.52-10.47	10	5.21	2.53-9.37
30-39	49	16.33	12.33-21.01	15	13.89	7.99-21.87	34	17.71	12.59-23.86
40-49	79	26.33	21.44-31.70	39	36.11	27.09-45.92	40	20.83	15.32-27.27
50-59	123	41.00	35.38-46.80	29	26.85	18.78-36.24	94	48.96	41.69-56.26
60-65	34	11.33	7.98-15.48	20	18.52	11.69-27.14	14	7.29	4.04-11.93
Total	300	100		108			192		

Table 2: Statistical HRV indicators (M ± m)

Indicator	Study group	Normal
HR beats/min	79.31 ± 3.27	60–80
RRNN (ms)	774.14 ± 30.75	800 ± 56
SDNN (ms)	29.74 ± 4.67	63 ± 35
RMSSD (ms)	20.42 ± 3.46	64 ± 6
pNN50%	5.09 ± 2.39	21.1 ± 5.1

HR beats/min is the heart rate, RRNN (ms) is the mean duration of all normal R-R intervals, RMSSD (ms) is the root mean square of the successive differences of all R-R intervals, SDNN (ms) is the standard deviation of R-R intervals, pNN50% is the number of adjacent intervals differing more than 50 ms expressed as a percentage of all the intervals in the collecting period.

Table 3: Spectral HRV indicators (M ± m)

Indicator	Study group	Normal
TP (ms^2)	1855.06 ± 647.4	3105 ± 1018
HF (ms^2)	301.83 ± 98.55	668 ± 203
LF (ms^2)	899.19 ± 398.14	1170 ± 416
VLF (ms^2)	330.68 ± 107.68	1267 ± 400
HF%	17.56 ± 3.31	15-45
LF%	36.12 ± 4.34	20-50
VLF%	21.82 ± 2.57	20-50
LF/HF	3.77 ± 0.92	1.5-2.0

TP is the total power, HF is the high frequency, LF is the low frequency, VLF is the very low frequency. They are determined when heart rate variability is plotted as a frequency at which the length of the R-R intervals changes.

The greatest number of patients (85.71%) was characterized by a low level of state anxiety, lack of tension, and nervousness at the time of the study. Only 7.14% of patients with high-level state anxiety were identified during the psychophysiological examination.

The study of preferred colors' positional frequency distribution in MetS patients (Table 5) showed the presence of color selecting specialties in the group.

In 37.5% of cases, red color did not occupy the first three positions, i.e., was rejected. There was a shift of yellow color to the eighth position of the color selection. More than half of the patients (56.3%) chose a green color for the first and second positions. Brown color appears on the second position in 31.25% of cases.

About 80% of the examined patients were characterized by a low level of CNS activation (Table 6).

Time reaction Me in this group was 321 msec (Q_{25}=313 msec; Q_{75}=337 msec). The standard deviation Me of the time reaction was 99 msec (Q_{25}=80 msec; Q_{75}=113 msec). Increases of the time reaction to visual triggers above 270 msec and its standard deviation values above 80 msec show inhibitory processes prevalence and reduced level of CNS functionality.

The remaining part of the patients (20%) showed average level of CNS activation and stable condition of regulatory mechanisms. Time reaction Me in this group was 287 msec (Q_{25}=278 msec; Q_{75}=290 msec). Time reaction standard deviation was 66 msec (Q_{25}=56 msec; Q_{75}=67 msec). No patients in the studied sample had a high level of CNS activation. Half of the examined patients showed moderate resistance of visual-motor reaction.

Table 4: Anxiety levels frequency distribution among MetS patients

Indicator		*n*	%	95% CI
Level of trait anxiety	No or low	8	11.11	5.07–21.25
	Moderate	19	27.78	16.73–37.56
	High	43	61.11	49.03–72.83
Level of state anxiety	No or low	60	85.71	75.29–92.93
	Moderate	5	7.14	2.36–15.89
	High	5	7.14	2.36–15.89

No or low anxiety level: STAI scores (20–37), moderate anxiety level: STAI scores (38–44), high anxiety level: STAI scores (45–80).

The statistical significant correlations between functional level of CNS activation and level of trait anxiety (r_s = –0.516, p = 0.002), and position of the yellow color (r_s = 0.581, p = 0.015) were identified in the study sample.

Table 5: Preferred colors' positional frequency distribution in MetS patients

Color	Position							
	1-st (%)	2-nd (%)	3-rd (%)	4-th (%)	5-th (%)	6-th (%)	7-th (%)	8-th (%)
1. Blue	6.25	6.25	6.25	18.75	50.00	12.50	0.00	0.00
2. Green	31.25	25.00	31.25	12.50	0.00	0.00	0.00	0.00
3. Red	31.25	18.75	12.50	6.25	6.25	12.50	6.25	6.25
4. Yellow	18.75	0.00	25.00	25.00	0.00	12.50	0.00	18.75
5. Violet	12.50	18.75	6.25	12.50	6.25	31.25	12.50	0.00
6. Brown	0.00	31.25	0.00	0.00	0.00	25.00	37.50	6.25
7. Black	0.00	0.00	6.25	6.25	12.50	0.00	18.75	56.25
0. Gray	0.00	0.00	12.50	18.75	25.00	6.25	25.00	12.50

PF in the study group was at a high level, Me of PF was 80 points, according to Table 7. Patients' physical condition did not prevent role-PF (RP) achievement – Me of RP was equal to 100 points.

Life quality is significantly affected by pain. According to the questionnaire, half of the patients had < 60 points on BP scale, while interquartile range (ΔQ) was from 41 to 100 points. This corresponds to patients' low GH level assessment. Me of GH was 52 points and ΔQ was from 45 to 62 points.

During mental health evaluation, it was found that the patients had a high level of fatigue and low vitality. Me of values on VT scale was 60 points.

Psychological health was average overall. Me of small dispersion MH scale was 68 points (ΔQ was from 52 to 80 points). At the same time, emotional condition was satisfactory and did not have a significant impact on the quality of daily activity, Me of RE was 100 points. High social activity (communication, spending time with friends, family, neighbors, and team) was observed to be preserved in the patients, which is traditional for Kazakhstan mentality (Me of SF was 87 points).

Discussion

Metabolic disorders were most frequent among 40–49 and 50–59 age groups. The main components of MetS were obesity and hypertension with predominating Grade 1 hypertension.

Table 6: Indicators of simple visual-motor reaction

Indicator		n	%	95% CI
Functional level of CNS activation	low	56	80.00	68.73–88.61
	moderate	14	20.00	11.39–31.27
	high	-	-	-
Reaction resistance	low	13	18.57	10.28–29.66
	moderate	35	50.00	37.80–62.20
	high	22	31.43	20.85–43.63

Heart rate is intricately regulated by complex interactions of multiple mechanisms, including sympathetic and parasympathetic nervous system, as well as hormonal homeostasis. HRV, which means variation of beat-to-beat interval, is a noninvasive way to evaluate cardiac ANS functions [37]. Given the potential mechanism underlying the development of MetS and its major cardiovascular complications, HRV is well recognized for its predictive power.

Table 7: Life quality domains in MetS patients according to SF-36 questionnaire

Domains		Me	Q_{25}	Q_{75}
Physical health	Physical functioning	80.0	60.00	95.0
	Role-physical functioning	100.0	75.00	100.0
	Bodily pain	62.0	41.00	100.0
	General health	52.0	45.00	62.0
Mental health	Vitality	60.0	47.50	75.0
	Role-emotional	100.0	66.00	100.0
	Mental health	68.0	52.00	80.0
	Social functioning	87.0	62.00	100.0

In the present study, several conventional parameters (SDNN, RMSSD, pNN50%) were able to distinguish MetS.

The clustering of various cardiovascular risks referred to as the MetS have led to the fact that patients with cardiovascular diseases often have one or more MetS components or undetected diabetes mellitus [38]. Cardiac dynamic alterations are associated with increased cardiovascular risk profile such as insulin-resistance, endothelial dysfunction, arterial stiffening, cardiac hypertrophy, and sympathetic activation [39]. Results from previous studies have shown that MetS factors by themselves, or in any combination, portend cardiovascular disease, and many other adverse outcomes [40].

Stuckey *et al*. [7] reviewed 14 investigations evaluating the relationship between HRV and MetS and found that high fasting plasma glucose (FPG) might be associated with decreased LF and HF, increased LF/HF ratio, along with neural effects on TP and VLF. The impact of FPG could be roughly interpreted as decreasing the parasympathetic tone and the mixture of both sympathetic and parasympathetic tone but not yet reaching the decrease of total autonomic tone. However, the results were not totally the same with our findings in which both sympathetic and parasympathetic tone, as well as total autonomic nervous tone, were decreased in MetS patients by means of significantly decreased values of VLF, LF, HF, and TP. It is possible that the humoral-metabolic component acquires all the more increasing role in heart rhythm regulation. The identified set of HRV indicators allows diagnosing neurocardiopathy due to systemic and local neurohormonal disorders.

It is a known fact that high trait anxiety correlates directly with neurotic conflict, emotional and neurotic breakdown, and psychosomatic diseases [41]. Moreover, at the high level of trait anxiety, clinical course of cardiovascular disease runs worse than at the average and low levels [42].

Several prior studies of MetS have documented that anxiety had a significant positive association with MetS [43], [44]. This study showed that high trait anxiety level but not state anxiety level accompanied MetS, as already reported earlier by Lemche *et al*. [45]. More than half of the patients had a high level of trait anxiety. Trait anxiety describes a stable tendency to perceive a large range of situations as a threat and to react with a state of anxiety. However, initially, anxiety is not a negative trait. A certain level of anxiety is a natural and necessary feature of active personality. In addition, trait anxiety characterizes vulnerability (or resilience) to influence of various stressors in general. Anxiety as a state (state anxiety) includes components such as subjective feelings of tension, anxiety, agitation, fear, and ANS activation. State anxiety is characterized by stress level at the time of the study. State anxiety of the same individual can vary at different times [46]. The greatest number of patients was characterized by a low level of state anxiety, lack of tension, and nervousness at the time of the study. However, a small number of patients with high-level state anxiety were revealed in this study. These patients were in a state characterized by subjective emotions, stress, anxiety, concern, and nervousness. It is possible that this state appeared as an emotional response to the situation caused by the medical check-up.

According to M. Lüscher's data, color choices "34215607" or "43251607" are close to average standard values and reflect an optimistic and cheerful personality position, absence of tension, anxiety, and stress [47]. The first position of the color selection corresponds to lead personal tendencies and predominant aspects of the motivational sphere. More than half of the patients chose a green color for the first and second positions. It follows from these color choices that rigidly introvert tendencies with the need to defend their own position, defensiveness, and aggressiveness of defensive nature were more common in the study group. Red color shift exposes emotional-vegetative tension, to the point of physiological and nervous exhaustion in the study sample. The choice of the yellow color as the last indicates anxiety and depression in addition to that. The choice of brown color, as the preferred color, characterizes the high level of anxiety and points to the need of anxiety reduction and the pursuit of psychological and physical comfort. In addition, brown on the second position reflects an anxiety problem, which has a vital (somatic) overtone and is associated with malaise, fatigue, and overexertion.

Examination of SVMR allowed revealing patients with persistent predominance of inhibition processes and a reduced level of CNS functional possibilities. Simultaneously the higher the level of trait anxiety and depression, the less functional level of CNS activation was in MetS patients.

MetS patients are active both in physical and social spheres. Their aspirations were explicitly expressed as communication, interaction with others, and social functions fulfillment. Bodily pain syndrome greatly influences MetS patients' life quality. The patients evaluate their health level as being low. A significant number of patients have noted a decline of vital energy. Emotional state of the patients did not affect the quality of their daily activities.

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