

Original Article

Association between Metabolic Syndrome and Health-related Quality of Life between Individuals with Normal and Impaired Glucose Regulation: Findings from Tehran Lipid and Glucose Study

Tina Deihim MD MPH¹, Parisa Amiri PhD¹, Hossein Hatami MD MPH², Leila Cheraghi MSc¹, Fereydoon Azizi MD³

Abstract

Background: Recent studies have shown that metabolic syndrome is associated with poor health-related quality of life (HRQoL). Moreover, it is shown that the prevalence of MetS and impaired glucose regulation, which are shown to have negative impact on HRQoL, overlap. This study aimed to investigate the association between HRQoL and metabolic syndrome (MetS) considering glucose regulation status in a sample of non-diabetic Tehranian adults.

Methods: This was a cross-sectional study conducted within the framework of the Tehran Lipid and Glucose Study (TLGS). Logistic regression analysis was used to estimate the odds ratio (OR) with 95% confidence interval (CIs) in normal and impaired glucose regulation. Cochran's Mantel-Haenszel test was used to test the homogeneity of the odds ratios for reporting poor HRQoL in those with MetS in two groups of normal and impaired glucose regulation.

Results: Totally, 946 participants were studied. After adjustment for age and educational level in women, MetS showed a significant negative impact on physical functioning and bodily pain in those with impaired glucose regulation and physical role limitation in normal glucose regulation group. In impaired glucose regulation group, women with MetS were more likely to report poor physical functioning (OR: 2.86, CI: 1.02-2.79), and bodily pain (OR: 2.96 CI: 1.09-8.04). In women with normal glucose regulation, poor physical role limitation was significantly associated with MetS. This association was not seen in men in either group. Based on the test of homogeneity of odds ratio, the association between MetS and HRQoL in those with normal and impaired glucose regulation was different in role physical subscale.

Conclusions: The current study showed that in both normal and impaired glucose regulation groups, MetS was associated with poor physical HRQoL in women but not men.

Keywords: Metabolic syndrome, quality of life, Glucose Intolerance

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Introduction

Health-related quality of life (HRQoL), an essential outcome measure to evaluate a patient's subjective sense of his/her physical and mental functioning and well being, has become an important outcome of care given for those with chronic diseases during the last two decades.¹ Metabolic syndrome (MetS) is a cluster of metabolic abnormalities including hypertension, dyslipidemia, impaired glucose tolerance and abdominal obesity which increase the risk of diabetes type 2, cardiovascular and chronic kidney diseases. Considering MetS as a chronic condition, the association between MetS and HRQoL

has been widely documented in recent years.²⁻⁶ Most previous studies have shown this association in women and mainly in the physical domains.^{2,7}

Despite the body of research on MetS and its association with cardiovascular outcomes, the concept of MetS is still under debate. Critical investigations have questioned whether MetS is a mere aggregation of metabolic abnormalities or a syndrome representing a clinical entity.⁸ Besides, the impact of MetS on poor HRQoL also is debatable. The different associations of some MetS components with HRQoL have been already demonstrated. Corica *et al.* showed body mass index (BMI), blood pressure and fasting plasma sugar to be the main correlates of poor physical HRQoL.³ However, high blood pressure was the only component of MetS that was associated with poor HRQoL among Korean men and women.⁶ There are also findings showing the strong negative effect of hyper-triglyceridemia, decreased HDL and high blood pressure but a weak effect of glucose level on HRQoL among a Latvian population.⁹ These controversies regarding the association between MetS component and HRQoL raise the question whether different patterns of MetS components could result in different effects on individuals' HRQoL.

It is not surprising that the prevalence of MetS and impaired

Authors' affiliations: ¹Research Center for Social Determinants of Endocrine Health and Obesity Research Center, Research Institute for Endocrine sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ²School of public health, Shahid Beheshti University of medical science, Tehran, Iran. ³Endocrine Research Center, Research Institute for Endocrine sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author and reprints: Parisa Amiri PhD, Research Center for Social Determinants of Endocrine Health and Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, P. O. Box: 19395-4763, Tel: +98 21 2409309, Fax: +98 21 2402463, Tehran, Iran. E-mail: amiri@endocrine.ac.ir
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glucose regulation, defined as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), overlap. Alexander *et al.* revealed that in a population of non-diabetic patients over 50 years of age, there were twice as many people with MetS and IFG than those with only IFG,¹⁰ consistent with the result of another study which also found MetS to be more prevalent in IFG and IGT patients.¹¹ Similarly recent studies have shown that impaired glucose metabolism is associated with reduced general health, physical, social functioning and increased pain dimensions.^{12,13} Considering this association, it seems reasonable to hypothesize that the association between MetS and HRQoL differs in normal individuals and those with impaired glucose regulation. To our knowledge, this is the first study aimed to investigate the association between MetS and HRQoL in those with and without impaired glucose regulation in a large sample of non-diabetic adults.

Materials and Methods

Subjects and Design

The current study was conducted within the framework of the Tehran Lipid and Glucose Study (TLGS). Details of the rationale and design of the TLGS have been published elsewhere.¹⁴ Briefly, to conduct the TLGS, three medical health centers in district 13 were selected from a total of 20 centers in eastern Tehran, under the surveillance of Shahid Beheshti University of Medical Sciences. More than 27,000 household members, registered at one of the three health centers for over three years, irrespective of their risk factors, were invited by telephone calls. The response rate was 55.5% (15,005 individuals). Thus, a total of 15005 individuals were selected through cluster random sampling. The TLGS has two major components: Phase 1 (1999 to 2001) was a cross-sectional prevalence study of non-communicable diseases (NCDs) and their associated risk factors; phase 2 is an ongoing prospective follow-up study in which NCD risk factors

are measured, approximately every 3 years. Following baseline collection of data, the intervention phase of the study was designed to improve lifestyles and prevent NCD risk factors.¹⁵

In this study, from the TLGS participants who completed the SF-36 questionnaire from September 2005 to September 2007, 1255 individuals, aged ≥ 20 were recruited for this study; of these 1255, 279 (22.2%) participants were diagnosed as diabetic and excluded from the study. Finally, after elimination of 30 (3.1%) participants with missing data, the information of 946 participants was analyzed (Figure 1). All participants were interviewed by a trained interviewer to collect data on HRQoL, socio-demographic information, physical activity, smoking habits, and medications used. All participants gave written informed consent. The study was approved by the ethics committee of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences.

Definitions

Metabolic syndrome was defined according to the Joint Interim Statement (JIS) criteria,¹⁶ which were at least 3 out of 5 criteria: 1) Elevated waist circumference ≥ 91 cm in women and ≥ 89 in men¹⁷; 2) reduced HDL-C < 50 mg/L in women, < 40 in men or on drug treatment for reduced HDL-C; 3) elevated triglyceride level ≥ 150 mg/dL or on drug treatment for elevated triglycerides; 4) elevated blood pressure (≥ 130 mmHg systolic blood pressure or ≥ 85 mmHg diastolic blood pressure) or on antihypertensive drug treatment in a patient with a history of hypertension and 5) elevated fasting glucose ≥ 100 mg/dL or on drug treatment for elevated glucose.

Smoking status was considered in two groups: 1) non- and ex-smokers and, 2) current smokers.¹⁸ Leisure time physical activity was measured based on hours of physical activity throughout the week.¹⁹ Diabetes was defined according to the criteria of the American Diabetes Association (ADA) as fasting plasma glucose ≥ 126 mg/dL or 2-h post 75 gram glucose load ≥ 200 mg/dL or

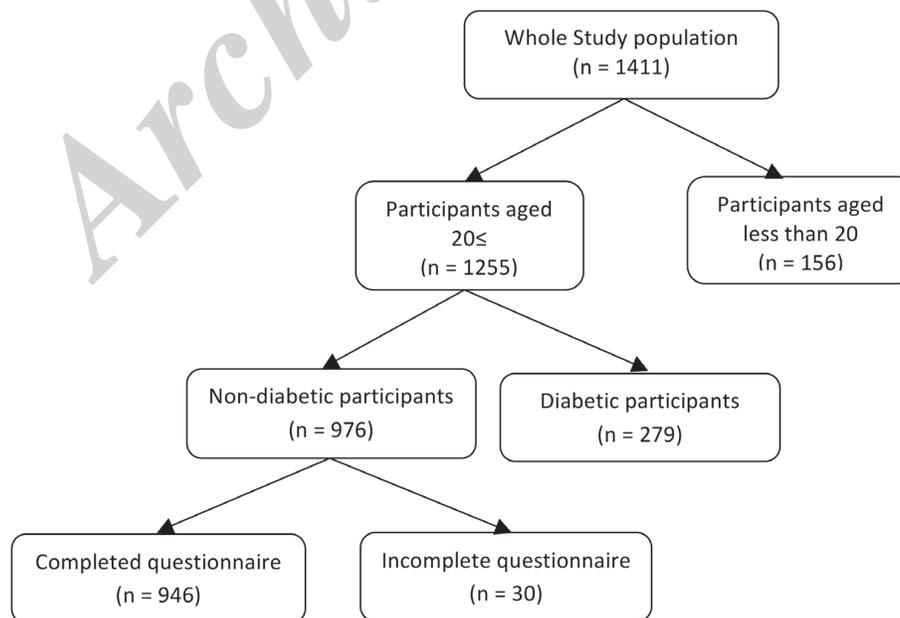


Figure 1. The sampling frame of study.

current therapy for a definite diagnosis of diabetes.²⁰ Impaired glucose regulation was defined according to the criteria of the American Diabetes Association (ADA) as fasting blood glucose ≥ 100 and < 126 or 2-h post 75 gram glucose load ≥ 140 and < 200 .²¹

Anthropometric measures

Waist circumference was measured at the umbilical level, over light clothing, using an unstretched tape meter, without any pressure to body surface and measurements were recorded to the nearest 0.1 cm. Blood pressure was measured twice, after participants were seated for 15 min, using a standard mercury sphygmomanometer; there was at least 30s interval between these two separate measurements and the mean of two measurements was taken as the blood pressure.

Laboratory measurements

Twelve-hour fasting blood samples were collected in tubes containing 0.1% EDTA and were centrifuged at 4°C and 500×g for 10 min, to separate the plasma. Blood glucose was measured on the day of blood collection by an enzymatic colorimetric method using glucose oxidase. Serum total cholesterol and triglyceride concentrations were measured with commercially available enzymatic reagents (Pars Azmoon, Tehran, Iran) adapted to a selectraautoanalyzer. HDL cholesterol was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungstic acid. Low density lipoprotein-cholesterol was calculated from serum total cholesterol, triglyceride (TG), and HDL-C, except when TG concentration was > 400 mg/dL.¹⁵

HRQoL measurement

Health-related quality of life was measured using the Iranian version of the Short Form Health Survey (SF-36), a widely used questionnaire that measures eight health-related concepts, including physical functioning, and role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health.²² The psychometric properties of the Iranian version of the SF-36 are well validated.²³ For each scale, a score ranging from 0 to 100 was considered as the worst and the best health conditions, respectively.

Statistical analysis

Continuous variables were checked for normality using graphical methods and they are expressed as mean \pm standard deviation (SD). Distribution of variables between two groups was compared using t-test except for TG and physical activity, for which Mann–Whitney test was used; categorical variables were compared using Pearson's χ^2 test or Fisher exact test and are reported as percentages.

Analysis of covariance (ANCOVA) was used to compare the mean scores of physical (physical functioning, physical role limitation, bodily pain and general health), and mental subscales (vitality, social functioning, role emotional and mental health) between patients with and without MetS in both the normal and impaired glucose regulation groups. Data were adjusted for age, education and physical activity.

Logistic regression analysis was used to estimate the odds ratio (OR) of poor HRQoL which has been defined as the 1st tertile of the physical or mental component summaries. Odds ratios (ORs) with 95% confidence intervals (CIs) were computed for

the normal and impaired glucose regulation groups for men and women separately; model 2 was adjusted for age, physical activity, smoking (Ref: Never or ex-smoking), education (Ref: above high school), and marital status (Ref: married). Due to the small population of smokers, smoking and marital status could not be adjusted in normal and impaired glucose regulation women for the role emotional and all subscales, respectively. This adjustment could not be considered in impaired glucose regulation men for the physical functioning subscale. Statistical analysis was performed using SPSS for Windows (version 15; SPSS Inc., Chicago, IL, USA), and significance was set at $P < 0.05$.

Cochran's Mantel-Haenszel test was used to test the homogeneity of odds ratios for reporting poor HRQoL in those with MetS in two groups of normal and impaired glucose regulation.

Results

The participants' general metabolic and clinical characteristics are presented in Table 1. The mean age of participants was 46.5 \pm 14.1 years and 64.3% (n = 608) were female. In the normal glucose regulation group, educational levels and the number of married individuals were significantly higher among subjects without MetS ($P < 0.001$). However, in the impaired glucose regulation group, there were no significant differences in educational level between those with or without MetS. In subjects with normal glucose regulation, the mean age of participants as well as the number of smokers was significantly higher in those with MetS. In both the impaired and normal glucose regulation groups, compared to those without MetS, those with this condition had higher mean levels of waist circumference (WC) ($P < 0.001$), body mass index (BMI) ($P < 0.001$), systolic and diastolic blood pressure ($P < 0.001$). In the normal glucose regulation group, FBS was significantly higher in those with MetS ($P < 0.001$); however, it was borderline in individuals with impaired glucose regulation ($P = 0.057$). Moreover, in both glucose regulation groups, those with MetS had significantly lower HDL-C level ($P < 0.001$) than those without MetS.

Overall, after adjustment for age and educational level, in those with impaired glucose regulation, subjects with MetS had lower scores in all SF-36 subscales except for physical role limitation in both genders and general health and role emotional only in men. Moreover, in women, MetS showed a significant negative association with physical functioning and bodily pain in those with impaired glucose regulation and physical role limitation in those with normal glucose regulation ($P < 0.05$); however, the association was borderline for physical functioning ($P < 0.07$) (Table 2).

Figure 2 shows the risk of being in the lowest tertile of each dimension of SF-36 questionnaire, based on glucose metabolism status. In subjects with impaired glucose regulation, only women with MetS had significant higher odds ratios for reporting poor physical functioning (OR: 2.86, CI: 1.02–7.99 $P < 0.05$) and bodily pain (OR: 2.96, CI: 1.09–8.04 $P < 0.05$) even after adjustment for age, sex, physical activity, smoking, education, and marital status. Among the normal glucose regulation group, women with MetS had significantly higher odds ratios for reporting poor HRQoL in physical functioning, physical role limitation, bodily pain and role emotional subscales; however, after adjustment for confounding factors, MetS could predict poor HRQoL in these women only in physical role limitation subscale (OR: 1.85, CI: 1.14–3.00 $P < 0.05$).

Table 1. Baseline characteristics of the study sample.

| | Impaired glucose regulation | | P-Value | Normal glucose regulation | | P-Value |
|--|-----------------------------|--------------------------|---------|---------------------------|---------------------------|---------|
| | With MetS (N = 172) | Without MetS (N = 52) | | With MetS (N = 271) | Without MetS (N = 451) | |
| Age (year) | 55.00 ± 12.20 | 53.71 ± 13.40 | 0.53 | 48.70 ± 13.22 | 41.24 ± 13.80 | 0.001 |
| Sex (male) | 60(34.9) | 22(42.3) | 0.33 | 116(42.8) | 140(31.0) | 0.001 |
| Education | | | 0.50 | | | 0.001 |
| Primary | 98(58) | 25(48.1) | | 127(47.6) | 153(33.9) | |
| Secondary | 57(33.7) | 22(42.3) | | 102(38.2) | 190(42.1) | |
| Higher | 14(8.3%) | 5(9.6%) | | 38(14.2) | 108(23.9) | |
| Marital status | | | 0.84 | | | 0.03 |
| Married | 138(80.2) | 41(78.8) | | 236(87.1) | 366(81.2) | |
| Single /Widowed/divorced | 34(19.8) | 11(21.2) | | 35(12.9) | 85(18.8) | |
| Smoking | | | 1.00 | | | 0.02 |
| Daily/occasional | 10(5.9) | 3(5.8) | | 34(12.8) | 33(7.3) | |
| Ex/never | 159(94.1) | 49(92.4) | | 232(87.2) | 418(92.7) | |
| MET-h/ wk | 13.11 ± 25.99 | 13.41 ± 18.57 | 0.10 | 12.88 ± 19.97 | 9.98 ± 16.23 | 0.08 |
| WC(cm) | 102.30 ± 10.00 | 92.92 ± 10.91 | 0.001 | 100.51 ± 8.33 | 86.64 ± 11.30 | 0.001 |
| BMI (kg/m ²) | 31.02 ± 4.24 | 28.22 ± 5.10 | 0.001 | 31.00 ± 4.50 | 26.52 ± 4.60 | 0.001 |
| TG (mg/dl) | 198(155,249) | 103(88.50,148) | 0.001 | 205(167,277) | 109(89,132) | 0.001 |
| Total cholesterol(mg/dL) | 204.10 ± 36.83 | 207.71 ± 40.80 | 0.22 | 211.22 ± 39.42 | 189.81 ± 35.61 | 0.001 |
| HDL-C (mg/dL) | 38.31 ± 8.50 | 49.54 ± 12.14 | 0.001 | 36.71 ± 7.11 | 46.10 ± 10.40 | 0.001 |
| LDL-C (mg/dL) | 125.14 ± 33.21 | 133.10 ± 33.83 | 0.16 | 129.80 ± 34.80 | 119.40 ± 31.10 | 0.001 |
| FBS (mg/dL) | 102.10 ± 9.20 | 99.31 ± 8.90 | 0.057 | 89.00 ± 5.82 | 86.04 ± 6.53 | 0.001 |
| SBP (mmHg) | 130.00 ± 19.00 | 118.04 ± 15.90 | 0.001 | 124.24 ± 17.00 | 109.80 ± 15.70 | 0.001 |
| DBP (mmHg) | 78.30 ± 10.13 | 75.02 ± 7.90 | 0.01 | 77.93 ± 10.10 | 70.62 ± 9.53 | 0.001 |
| 2h-BS(mg/dL) | 141.68 ± 31.68 | 140.79 ± 30.52 | 0.85 | 100.01 ± 20.90 | 94.00 ± 19.52 | 0.001 |
| Data are presented as Mean ± SD or N (%) | | | | | | |
| TG is presented as median (Q1-Q3) | | | | | | |
| WC = waist circumference; BMI = body mass index; TG = triglycerides; HDL-C = high density lipoprotein-cholesterol; LDL-C = low density lipoprotein-cholesterol; FBS = fasting blood sugar; SBP = systolic blood pressure; DBP = diastolic blood pressure. P < 0.05 has been considered significant | | | | | | |

Based on Cochran's Mantel-Haenszel test (test of homogeneity of odds ratio), the association between MetS and HRQoL in those with normal and impaired glucose regulation was different in role physical subscale only in women ($P = 0.02$).

Discussion

The current study showed that in both the normal and the impaired glucose regulation groups, MetS was associated with poor physical HRQoL in women, but not in men; in impaired glucose regulation women, MetS could predict poor physical functioning and bodily pain even after adjusting for potential confounders; however, in those with normal glucose regulation, only physical role limitation was significantly associated with MetS. There were no significant associations between MetS and mental HRQoL, either the normal or impaired glucose regulation groups.

To compare HRQoL in those with and without MetS stratified by individuals' glucose regulation status, our results showed that MetS was associated with physical role limitation in normal; and physical functioning and bodily pain in the impaired glucose regulation group. This difference between the association of MetS and HRQoL in the two mentioned groups could be due to significant diverse associations of IFG with physical functioning, general health and bodily pain.^{24,25} However, other findings show

an insignificant difference between the HRQoL reports among normal and impaired fasting glucose individuals.⁶ The association between IFG and IGT with pain may be due to poly-neuropathy which is slightly more prevalent in these patients, compared to individuals with normal glucose regulation^{26,27}; this discrepancy may be due to IGT status, the negative significant association of which with general health, physical and social functioning has been previously demonstrated among Australians; although there was no association between IFG and any domains of HRQoL.¹²

Consistent with previous studies, our results showed a sex-dependent association between MetS and poor HRQoL only in women and in both the impaired and the normal glucose regulation groups. Park *et al.* concluded that greater impairment of HRQoL due to MetS in women may be related to the lower socio-demographic status of women and psychological distress related to abnormal body shape.⁶ Moreover, gender differences related to chronic disease could be due to lower immune function, psychological factors, social inequality and biochemical factors²⁸; consequently, the association between MetS and cardiovascular disease was also more pronounced in women.²⁹ Saltevo *et al.* stated that higher inflammatory stress in women compared to men with prediabetes and diabetes type 2 may explain the higher rates of cardiovascular events in women.³⁰ Furthermore, the association between MetS and HRQoL in the present study was mainly evident in the physical domains in both the normal and impaired glucose regulation groups. In women with impaired and normal glucose

Table 2. Gender specific SF-36 scores in those with and without impaired glucose based on their metabolic syndrome status.

| | Men | | | | Women | | | |
|---------------------------------|-----------------------------|--------------------------|---------------------------|---------------------------|-----------------------------|--------------------------|---------------------------|---------------------------|
| | Impaired glucose regulation | | Normal glucose regulation | | Impaired glucose regulation | | Normal glucose regulation | |
| | With MetS (N = 60) | Without MetS (N = 22) | With MetS (N = 116) | Without MetS (N = 140) | With MetS (N = 112) | Without MetS (N = 30) | With MetS (N = 155) | Without MetS (N = 311) |
| Physical functioning | 76.07(24.20) | 79.97(21.75) | 84.51(19.16) | 85.36(19.03) | 67.76(39.83) | 80.16(32.26)* | 74.54(22.93) | 78.61(22.25) |
| Physical role limitation | 76.83(41.34) | 61.44(37.16) | 76.06(33.07) | 75.24(32.84) | 61.27(57.94) | 59.20(46.93) | 59.09(39.93) | 68.29(38.74)* |
| Bodily pain | 75.82(17.52) | 76.82(15.75) | 77.39(16.56) | 76.46(16.45) | 68.80(36.89) | 80.96(29.88)* | 67.33(20.62) | 70.62(20.01) |
| General health | 65.28(23.74) | 61.28(21.33) | 68.31(17.83) | 69.79(17.70) | 59.07(30.31) | 63.90(24.55) | 61.36(20.17) | 63.48(19.57) |
| Vitality | 64.07(23.31) | 64.62(20.95) | 68.08(17.94) | 68.78(17.81) | 61.14(36.19) | 65.89(29.31) | 57.06(22.09) | 57.47(21.43) |
| Social functioning | 74.29(29.24) | 77.53(26.28) | 78.39(21.28) | 77.61(21.13) | 69.62(39.62) | 78.94(32.08) | 73.08(25.30) | 74.67(24.55) |
| Role emotional | 69.61(49.65) | 60.93(44.62) | 67.74(37.61) | 70.16(37.34) | 57.71(64.01) | 62.54(51.84) | 63.80(43.59) | 62.43(42.29) |
| Mental health | 67.91(23.21) | 70.44(20.86) | 70.22(18.04) | 73.08(17.91) | 65.61(34.48) | 68.40(27.92) | 63.08(21.37) | 65.51(20.74) |

Data are presented as mean (SD), and adjusted for age, education level and physical activity. MetS = metabolic syndrome is defined based on the joint interim statement (JIS).¹⁶
 *P < 0.05 between those with and without metabolic syndrome

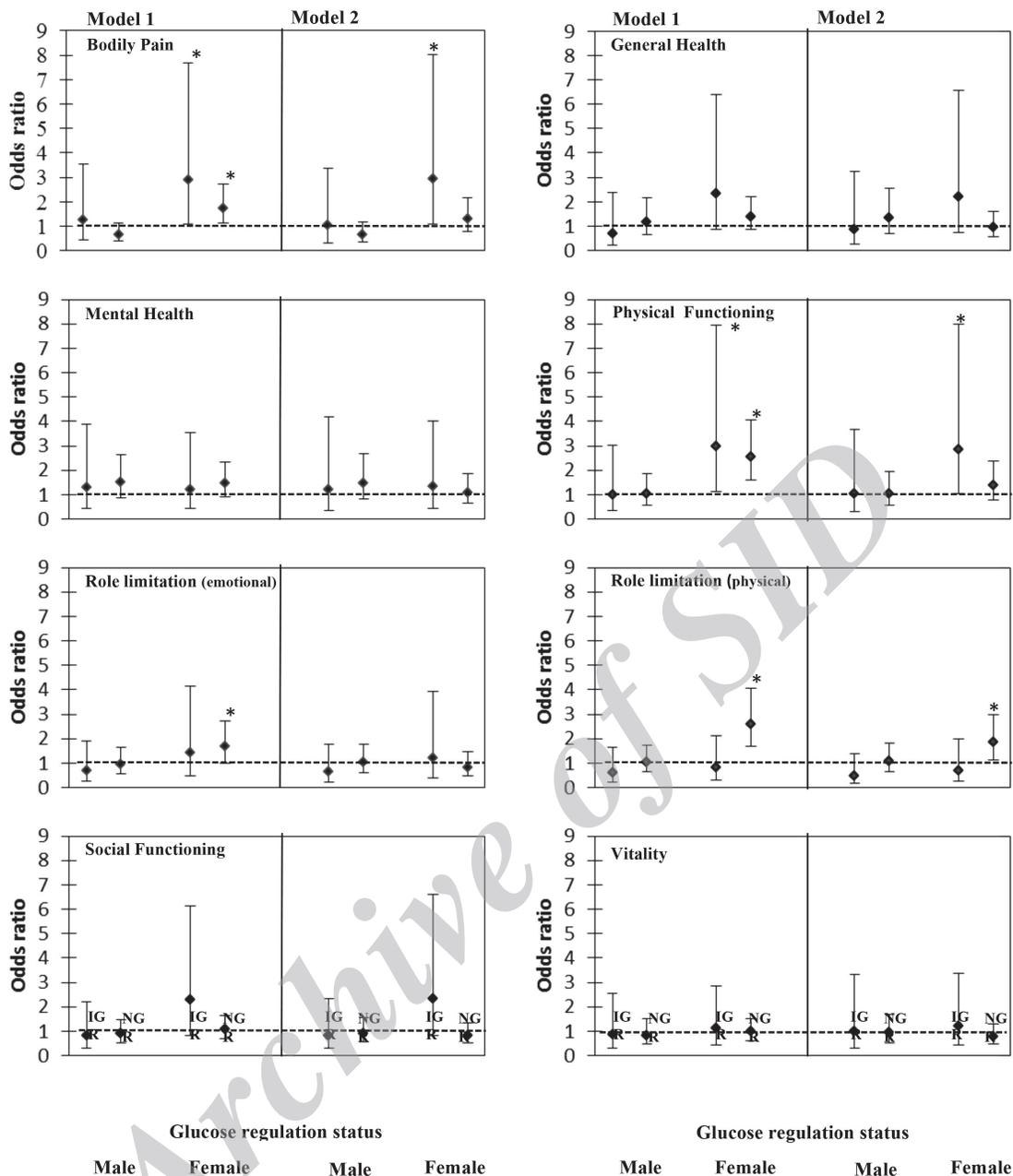


Figure 2. Sex-specific adjusted odds ratios for reporting poor health-related quality of life in those with MetS in both normal and impaired glucose regulation groups by genders.

Model 1: Unadjusted

Model 2: Data adjusted for Age, physical activity, smoking (Ref: Never or ex-smoking), education (Ref: Above high school education), marital status (Ref: Married)

IGR = impaired glucose regulation (impaired fasting glucose or impaired glucose tolerance), NGR = normal glucose regulation

* $P < 0.05$

regulation, those with MetS reported difficulty in performing physical tasks and physical role limitation, respectively. Our results are consistent with previous studies that showed more physical limitation in subjects with MetS.³¹ Moreover, a study conducted in older adults demonstrated MetS to be a distinct and significant risk factor for mobility restriction.³²

To the best of our knowledge, this is the first report comparing

the association between MetS and HRQoL in impaired and normal glucose regulation subjects in a large sample of non-diabetic adults. To mention the study limitations, there may be more unmeasured confounding factors such as economic status that could affect HRQoL, factors which we did not adjust for. Due to sample limitation, results of physical functioning could not be adjusted for marital status in men, as well as smoking in women

with impaired glucose regulation. Finally, the cross-sectional design did not allow us to investigate the directionality of the correlation between study variables and HRQoL.

In conclusion the association between MetS and HRQoL differs between individuals with impaired and those with normal glucose regulation, but only in women and in the physical domain. After adjustment for confounding variables, women with MetS have a significantly higher odds ratio for reporting poor HRQoL in physical functioning and bodily pain subscales in impaired glucose regulation group, compared with their normal metabolic counterparts. This is an important finding which indicates that future health policies should consider the association between MetS and HRQoL in different high risk groups. In our study, due to sample limitations, we could not analyze the association of MetS with HRQoL in the IFG and IGT groups separately. Larger studies should be done to evaluate the association separately between MetS and poor HRQoL in IFG and IGT groups.

Conflict of interests

The authors have not declared any conflicts of interest.

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