Reprinted from the German Journal of Psychiatry http://www.gjpsy.uni-goettingen.de ISSN 1433-1055

Prevalence of the Metabolic Syndrome in Substance-Dependent Men

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Abstract

Background: Substance abuse, alcohol in particular, is associated with increased risk of diabetes and metabolic syndrome (MS). The relationship between the substance abuse and MS is complex and the literature is sparse. Objective: The present research was aimed to study the prevalence and predictors of MS among inpatients with substance dependence.
Method: The study was conducted in tertiary care centre in North India, in which all consecutive patients with substance dependence were recruited, who were admitted from 1st January, 2011 to 31st December, 2011. MS was assessed using International Diabetes Federation (IDF) and Modified NCEP ATP-III criteria.
Results: Out of 256 subjects, 24 (9.4%) subjects met the IDF criteria and 28 (10.9%) subjects met the modified NCEP criteria for MS with higher prevalence of MS in patients with alcohol and opioid dependence (26.7%) compared to alcohol (13.1%) or opioid dependence (9.6%). The commonest abnormalities were increased triglycerides (37.5%) and increased blood pressure (33.6%). On regression analysis, body mass index was found to be the most significant predictor for the development of MS.
Conclusions: MS was highest in subjects with alcohol and opioid dependence with the commonest abnormality of triglyceride and blood pressure. Hence routine screening is advisable in this population to address emerging MS (German J Psychiatry 2013; 16(2): 61-67).

Keywords: metabolic syndrome, substance dependence, alcohol, opioid

Received: 31.7.2012
Revised version: 12.2.2013
Published: 1.8.2013

Introduction

Metabolic Syndrome (MS), also known as Syndrome X, Reaven syndrome and Deadly quartet, is characterized by poorly understood complex biological mechanisms at the cellular level (Leslie, 2005). Substance dependence increases the risk of developing the metabolic syndrome by increasing cell damage, augmenting excitotoxicity, reducing energy production, and lowering the antioxidant potential of the cells (Virmani et al., 2007).

The aetiology of the metabolic syndrome is complex, determined by the interplay of both genetic and environmental factors (Ala et al, 2009). Alcohol is a significant source of calories, with its inherent properties as well as by stimulating appetite (Calissendorff et al., 2005) and greater consumption of fatty products (cheese, meat) in drinkers. An association between alcohol consumption and a greater waist circumference has been consistently reported (Buja et al., 2010).

Alcohol and tobacco use, in particular, have been associated with increased risk of developing metabolic syndrome which is further worsened by nutritional deficiency (Athyros et al., 2008; Baik & Shin, 2008; Weitzman et al., 2005). Though their relationship remains complex as low to moderate alcohol use has been found to lower the risk for MS (Athyros et al., 2008; Carnethon et al., 2004; Djousse et al., 2004; Freiberg et al., 2004; Gigleux et al., 2006; Lidfeldt et al., 2003; Yoon et al., 2004), while heavy alcohol use has been found to increase the risk for MS (Athyros et al., 2008; Baik & Shin, 2008; Fan et al., 2006; Freiberg et al., 2004; Urashima et al., 2005). Some studies have reported a negative rela-

tionship between low alcohol use and MS in men (Djousse et al., 2004) and in women (Wilsgaard & Jacobsen, 2007; Zhu et al., 2004).

The prevalence of MS in substance dependent population have been reported in the range of 5-31% (Djousse et al., 2004; Gigleux et al., 2006; Rosell et al., 2003; Santos et al., 2007; Teixeira & Rocha, 2007; Urashima et al., 2005; Villegas et al., 2004; Yoon et al., 2004; Zhu et al., 2004). Reduced levels of high density lipoprotein cholesterol (Kanjilal et al., 2008; Pereska et al., 2011), increased levels of triglycerides (Pereska et al., 2011) and increased BMI (Kanjilal et al., 2008) were significantly found to contribute to MS.

Research from India on MS and substance abuse is limited to only one study from North India (Mattoo et al., 2011). The present research was aimed to study the prevalence and predictors of Metabolic Syndrome among inpatients with substance dependence.

Methods

The study was conducted at the Drug De-addiction and Treatment Centre (DDTC), Department of Psychiatry, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh - a multispecialty tertiary-care teaching hospital providing services to a major area of north India. Most DDTC patients come by family or self-referral, and some are referred from other hospitals or other departments of our Institute. The services are run by a team of psychiatrists, social workers, clinical psychologists, and nurses. The services include outpatient, inpatient, basic laboratory, active and passive aftercare/follow up, and liaison with governmental and non-governmental agencies and self-help groups. The assessments include comprehensive physical and psychosocial evaluation, including for physical and psychiatric comorbidities. The treatment modalities used include pharmacotherapy, psycho-behavioural therapies, and social-occupational rehabilitation.

The study had the approval of the institutional research ethics committee. All consecutive patients, who were admitted to the inpatient unit from 1st January, 2011 to 31st December, 2011 were recruited. A cross-sectional design was used. A written informed consent was obtained from the patients taken up for the study as well as from the parents of the patients < 18 years age. Total admissions were 256 in above specified period and all were included. Diagnoses were made as per International Classification of Diseases - Classification of Mental and Behavioural Disorders - Clinical Descriptions and Diagnostic Guidelines tenth revision (ICD-10) (WHO, 1992). All of our patients were males as because of lack separate facilities in this centre. We admit female substance users in psychiatric inpatient unit under the same department. After enrolment into the study, a semi-structured proforma was used to assess demographic and substance use details.

Metabolic and anthropometric assessments

Body weight was measured in kilogram (kg) and height in centimeters (cm) by a calibrated scale. Waist circumference, in centimeters (cm), was measured midway between the inferior costal margin and the superior border of the iliac crest, at the end of normal expiration in standing position. At least two readings at 5-minute intervals were recorded for Blood pressure (BP) using standard mercury manometer in supine position. If blood pressure was found to be high (≥140/90) then a third reading was taken after 30 minutes; the lowest of these readings was taken. Fasting venous blood sample was collected under aseptic condition to measure the blood glucose (FBS), triglycerides (TG) and high density lipoprotein (HDL) levels.

A number of expert groups have developed clinical criteria for defining MS. The most widely accepted of these have been given by the National Cholesterol Education Program – Third Adult Treatment Panel (NCEP ATP-III) (2001) and International Diabetes Federation (IDF) (Alberti et al., 2005). According to International Diabetes Federation (IDF) criteria a person is considered to have metabolic syndrome if he has high waist circumference (≥ 80 cm for females and ≥ 90 for males of Asian origin) along with 2 of the following criteria: systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥85 mm of Hg (or on treatment for hypertension), triglyceride levels ≥ 150 mg/dl (or on specific treatment for this abnormality), HDL cholesterol < 40 mg/dl for male and <50 mg/dl for females (or on specific treatment for this abnormality), fasting blood sugar ≥ 100 mg/dl (or on treatment for diabetes mellitus) (Alberti et al., 2005). According to NCEP ATP-III, the cutoffs are similar with respect to specific abnormalities as defined by IDF, except that the waist circumference (≥ 88 cm for females and ≥ 102 for males) criteria is different and it is not mandatory and presence of any of the 3 is sufficient (Executive summary of the third report of NCEP, 2001). According to modified NCEP ATP-III criteria, the waist circumference criteria for Asians are relaxed to ≥ 90 cm for males and ≥ 80 for females (Tan et al., 2004; Misra et al., 2005; Heng et al., 2006).

Metabolic syndrome was diagnosed using both IDF criteria (Alberti et al., 2005) and modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) criteria (Executive summary of the third report of NCEP, 2001; Tan et al, 2004; Misra et al., 2005; Heng et al., 2009).

Ethical issues

All patients and healthy controls with metabolic abnormalities were informed and educated about the need for proper diet and regular exercise, and referred for specialist care whenever required.

Table 1. Sociodemographic and clinical profile

Variable	Total sample (N=256)	Alcohol (N=107)	Opioid (N=100)	Alcohol+ opioid (N=30)	χ2 / F value
	Mean (SD)				
Age (years)	34.24 (10.25)	40.07 (10.20)	28.59 (7.03)	32.97 (7.31)	45.97***
Education (years)	11.69(4.48)	11.81 (5.81)	11.71 (3.42)	11.57 (2.92)	0.037
Duration of dependence (years)	10.47 (6.55)	12.91 (6.99)	7.84 (4.68)	10.88 (6.86)	17.81***
	Frequency (%)				
Marital status					
Single	89 (34.8)	20 (18.7)	53 (53)	9 (30)	27.21***
Married	167 (65.2)	87 (81.3)	47 (47)	21 (70)	
Occupational status					
Working	148 (57.8)	73 (68.2)	43 (43)	22 (73.3)	16.74***
Not working	108 (42.2)	34 (31.8)	57 (57)	8 (26.7)	
Religion					
Hindu	154 (60.2)	73 (68.2)	52 (52)	13 (43.3)	10.32
Sikh	96 (37.5)	33 (30.8)	44 (44)	16 (53.3)	
Others	6 (2.4)	1 (0.9)	4 (4)	1 (3.3)	
Family type					
Nuclear	161 (62.9)	70 (65.4)	60 (60)	17 (56.7)	1.06
Extended/ Joint	95 (37.1)	37 (34.6)	40 (40)	13 (43.3)	
Locality					
Urban	177 (69.1)	80 (74.8)	64 (64)	20 (66.7)	2.91
Rural	79 (30.9)	27 (25.2)	36 (36)	10 (33.3)	
Tobacco dependence	184 (71.9)	73 (68.2)	77 (77)	23 (76.7)	2.25
Physical disorder[1]	98 (38.3)	45 (42.1)	38 (38)	12 (40)	0.35
Psychiatric disorder[2]	33 (12.9)	13 (12.1)	10 (10)	6 (20)	2.15

***p<0.001

[1]Physical comorbidity: Seizure disorder–44 (17.2) [GTCS– 42 (16.4), partial–2 (0.8)], Hepatitis C–10, Heamorrhoids–2, pityriasis versicolor–1, psoriasis–2, sinus bradycardia–2, spinal cord compression–1, neuropathy–1, pancreatitis–1, coronary artery disease–1, cirrhosis–1, diabetes mellitus–8, essential tremors–1, fistula in ano–1, gall stone–1, hepatitis B–4, HIV positive–1, hypertension–12, irritable bowel syndrome–1, migraine–2, osteoarthritis–1, Parkinson's disease–1, prolapsed intervertebral disc– 1, tuberculosis–2, deep vein thrombosis–1, gastroesophageal reflux disease–1, cataract–1

[2]Psychiatric comorbidity: Recurrent depressive disorder–5, bipolar disorder–6, attention deficit hyperkinetic disorder–3, social phobia–2, schizophrenia–4, adjustment disorder–2, dysthymia–3, panic disorder–2, psychosis unspecified–2, generalized anxiety disorder–1, mild mental retardation–1, dissociative disorder–1, deliberate self-harm–1, periodic limb movement disorder–1, erectile dysfunction–1, premature ejaculation–1

Statistical analysis

Analysis was done using the SPSS version 14.0 for Windows (Chicago, Illinois, USA). Frequencies with percentages were calculated for categorical variables and mean and standard deviation were calculated for continuous variables. Chi-Square test, t-tests and one way ANOVA were used for comparisons. Binary logistic regression was performed to examine the influence of independent variables on MS.

Results

Demographic and clinical details

A total of 256 subjects, all men, were included in the study. The commonest substance dependence was of tobacco (N=184, 71.9%), followed by alcohol (N=133, 52%) and opioids (N=126, 49.2%), while sedatives (N=32, 12.5%), cannabis (N=21, 8.2%) and volatiles dependence (N=3, 1.2%) were reported less commonly. On the basis of main substance of intake we grouped our patients in to four groups: alcohol (N=107), opioid (N=100), alcohol and opioid(N=30), and others (N=49). Other subgroup consist patients with intake of other main substance, or multiple substances, or with less clear pattern and information. Thus it being a heterogeneous group, we omitted it from comparison of first three groups. Our typical study subject was aged

Table 2. MS definition

Variable	Total sample (N=256)	Alcohol (N=107)	Opioid (N=100)	Alcohol+ opioid(N=30)	χ^2/F value
	Mean (SD)				
Body Weight (kg)	64.16 (11.82)	63.75 (11.16)	63.51 (12.85)	68.2 (12.49)	1.88
Height (cm)	168.60 (6.32)	167.60 (6.09)	169.07 (6.66)	170.1 (6.23)	2.41
Body mass index	22.58 (4.05)	22.75 (4.17)	22.15 (3.91)	23.62 (4.42)	1.60
Waist circumference (cm)	83 (8.43)	83.86 (7.45)	81.3 (9.46)	85.33 (8.92)	3.65*
Systolic BP (mm Hg)	119.68 (10.99)	120.05(11.99)	119.46 (9.88)	119.26(10.82)	0.103
Diastolic BP (mm Hg)	78.13 (7.44)	78.84 (8.32)	77.16 (6.78)	78.26 (6.29)	1.32
HDL levels (mg/dl)	59.13 (26.79)	60.57 (26.07)	59.59 (30.22)	52.54 (17.42)	1.05
Triglyceride (mg/dl)	144.27 (48.41)	141.6 (51.29)	148.09(49.68)	148.6 (45.82)	0.513
Total Cholesterol (mg/dl)	164.51 (42.98)	169.41(46.36)	161.49(43.16)	168.56(31.67)	0.830
LDL levels (mg/dl)	84.24 (35.44)	82.55 (40.03)	84.23 (34.73)	89.99 (26.38)	0.381
Fasting blood Glucose (mg/dl)	91.37 (21.67)	90.87 (14.17)	90.63 (40.38)	99.16 (40.38)	1.86
	Frequency (%)				
Systolic BP ≥130 mm Hg	77 (30.1)	37 (34.6)	24 (24)	11 (36.7)	3.37
Diastolic BP ≥85 mm Hg	44 (17.2)	26 (24.3)	11 (11)	5 (16.7)	6.29*
Abnormal BP (≥130//≥85) or diagnosed as hypertensive	86 (33.6)	44 (41.1)	25 (25)	12 (40)	6.49*
Triglyceride levels ≥150 mg or on lipid lowering agents	96 (37.5)	38 (35.5)	40 (40)	15 (50)	2.10
Lower HDL (<40 mg) or on lipid lowering agents	28 (10.9)	15 (14)	7 (7)	5 (16.7)	3.46
Fasting blood Glucose ≥100 mg % or diagnosed as diabetes	30 (11.7)	15 (14)	8 (8)	7 (23.3)	5.23
Abnormal Waist circumference (≥90 cm)	49 (19.1)	21 (19.6)	16 (16)	9 (30)	2.89
Obesity (BMI ≥25)	62 (24.2)	28 (26.2)	18 (18)	13 (43.3)	8.09*
MS (IDF)	24 (9.4)	13 (12.1)	5 (5)	6 (20)	6.58*
MS (modified NCEP ATP-III)	28 (10.9)	14 (13.1)	6 (6)	8 (26.7)	9.76**
MS components					
0	97 (37.9)	36 (33.6)	39 (39)	10 (33.3)	13.99
1	74 (28.9)	33 (30.8)	35 (35)	4 (13.3)	
2	57 (22.3)	24 (22.4)	20 (20)	8 (26.7)	
3	16 (6.3)	7 (6.5)	4 (4)	5 (16.7)	
4	8 (3.1)	5 (4.7)	1 (1)	2 (6.7)	
5	4 (1.6)	2 (1.9)	1 (1)	1 (3.3)	

*p<0.05; **p<0.01

34.24 years, married (65.2%), working (57.8%), from urban area (69.1%), Hindu (60.2%), from nuclear family (62.9%) with the mean education of 11.69 years and 10.47 years of substance dependence. Nearly one-third patients were also having comorbid physical disorder, while psychiatric comorbidity was less common (12.9%).

Compared to others, alcohol group was significantly older (p<0.001), married (p<0.001), and taking substance for longer duration (p<0.001) while alcohol and opioid group was significantly more employed (p<0.001). The three groups were similar for education, religion, family type, locality and presence of tobacco dependence, comorbid physical and psychiatric disorders. Further information about individual groups and physical and psychiatric comorbidities are detailed in Table 1.

Metabolic parameters

Details of the anthropometric findings and physical examination findings and biochemical profile are shown in Table 2. Mean waist circumference and obesity were significantly higher in the alcohol and opioid group than alcohol and opioid groups (p<0.05). Abnormal diastolic blood pressure was significantly higher in alcohol group (p<0.05) and abnormal blood pressure was significantly lesser in opioid group (p<0.05).

Although there was no significant difference in the prevalence of other individual parameters used to define MS, higher percentage of patients in alcohol and opioid group fulfilled criteria of abnormal systolic blood pressure, low levels of high density lipoprotein (HDL), high levels of triglyceride, high fasting blood sugar level and higher waist circumference (see Table 2).

Significantly higher percentage of patients in alcohol and opioid group had MS when compared to patients in alcohol and opioid group, according to both IDF (20% vs 12.5% and 5%, p<0.05) and modified NCEP-ATP III criteria (26.7% vs 13.1% and 6%, p<0.001). There was high concordance between IDF and modified NCEP-ATP III criteria for MS for the entire sample (N=256) (kappa value- 0.895, p<0.001). Half of the subjects in entire sample were fulfilling one or two MS components.

Table 3: Predictors of MS

Variable	Criteria	B	SE	df	Wald	Odds Ratio	p	Confidence interval
Age	IDF Criteria	0.087	0.019	1	20.01	1.09	<0.001	1.05–1.13
Education		0.133	0.056	1	5.63	1.14	0.018	1.02–1.27
Married		1.88	0.75	1	6.31	6.60	0.012	1.51–28.75
Duration of dependence		0.082	0.028	1	8.98	1.08	0.003	1.02–1.14
Weight		0.080	0.018	1	18.77	1.08	<0.001	1.04–1.12
Body mass index		0.280	0.057	1	23.77	1.32	<0.001	1.18–1.48
Body mass index ≥ 25		2.55	0.50	1	26.0	12.8	<0.001	4.80–34.17
Physical comorbidity		0.903	0.436	1	4.28	2.46	0.038	1.05–5.79
Age	Modified NCEP ATP–III criteria	0.073	0.018	1	16.70	1.07	<0.001	1.03–1.11
Education		0.154	0.058	1	7.18	1.16	0.007	1.04–1.30
Married		1.27	0.55	1	5.20	3.56	0.022	1.19–10.62
Duration of dependence		0.084	0.026	1	10.19	1.088	0.001	1.03–1.14
Weight		0.074	0.017	1	18.39	1.07	<0.001	1.04–1.11
Body mass index		0.243	0.052	1	21.96	1.27	<0.001	1.15–1.41
Body mass index ≥ 25		2.01	0.429	1	22.17	7.52	<0.001	3.24–17.43
Physical comorbidity		1.031	0.411	1	6.29	2.80	0.012	1.25–6.27

On comparing patients with MS (N=24) (IDF criteria) with those without MS (N=232), it was seen that higher percentage of those with MS were older (44.13±10.80 vs. 33.22±9.65; t = -5.21, p<0.001), married (91.7% vs. 62.5%, χ^2 8.15, p<0.01), more educated 14.79±9.32 vs. 11.37±3.52; t value -3.64, p<0.001), had longer duration of illness (91.6± 66.6 vs. 65.71 ± 66.0; t = 2.11, p<0.05), had greater physical comorbidity (58.3% vs. 36.2%, χ^2 4.50, p<0.05), had higher body weight (75.35±11.11 vs. 57.72±10.68; t = 9.16, p<0.001), had higher body mass index (27.94 ± 4.46 vs. 21.64 ± 3.57; t = 9.08, p<0.001) and higher percentage of patients were obese (BMI ≥25) (75% vs. 19%, χ^2 = 37.21, p<0.001).

When similar comparisons were made using modified NCEP ATP III criteria, those with MS differed from those without MS on the same variables as noted when IDF criteria were applied.

Predictors of metabolic syndrome

Simple binary logistic regression analysis with enter method was used to study the relationship among independent variables which were more frequently present in subjects with MS in either group. As shown in Table 3, in entire sample (N=256) significant predictors of MS according to IDF criteria were being older, higher education, greater duration of dependence, presence of physical comorbidity, higher body weight, higher body mass index and body mass index ≥25. When MS was defined by modified NCEP ATP-III, same variables emerged as the predictors. Of all predictors, odds ratio was highest for BMI ≥25 (see Table 3).

Discussion

Alcohol and tobacco use have been associated with increased risk of diabetes (Baik & Shin, 2008; Wannamethee et al., 2001), cardiovascular mortality (Athyros et al., 2008; Ocekene & Miller, 1997), and the development of metabolic syndrome (Athyros et al., 2008; Baik and Shin, 2008; Weitzman et al., 2005), which in turn is an important risk factor for cardiovascular diseases and all-cause mortality (Isomaa et al., 2002 & Lakka et al., 2002).

Our typical study subject was a married, working, male in forth decade from Hindu nuclear family of urban area with the mean education of 11.69 years and 10.47 years of substance dependence. The demographic profile of our sample was similar to that of our clinic population (Basu et al., 2012, Mattoo et al., 2011). All the subjects being male are due to the admission policy of our institute. Further, very few females actually seek treatment for substance use disorders at our center, in our region and in India (UNODC ROSA and MSJE, 2002; Grover et al., 2005; Basu et al., 2011).

There was high concordance between IDF and modified NCEP-ATP III criteria for MS for the entire sample. The prevalence rate of MS in entire study sample was 9.4% by IDF criteria and 10.9% by modified NCEP ATP-III. 12.1% (IDF) and 14% (modified NCEP ATP-III) MS in the patients with alcohol dependence was within the range of 5-31% reported for subjects taking alcohol by the Western studies (Djousse et al., 2004; Gigleux et al., 2006; Rosell et al., 2003; Santos, 2007; Teixeira & Rocha, 2007; Urashima et al., 2005; Villegas et al., 2004; Yoon et al., 2004; Zhu et al., 2004). The prevalence of MS in the patients with opioid dependence in our study was 5% (IDF) and 6% (modified NCEP ATP-III) was lower than earlier study (Mattoo et al., 2011).

The prevalence of MS was found to be much higher in the group dependent on alcohol and opioids both (20% by IDF and 26.7% by modified NCEP ATP-III criteria) compared to alcohol only and opioid only subjects suggesting contributory effect of both opioids and alcohol.

On analysis of various components, we found that waist circumference and obesity were significantly higher in the alcohol and opioid group than alcohol and opioid groups. Abnormal diastolic blood pressure was significantly higher in alcohol group and abnormal blood pressure was significantly lesser in opioid group.

Overall, when compared with those without MS, the subjects with MS in all groups were of significantly higher age, more likely to be married, more educated, had longer duration of illness and greater physical comorbidity. They also had higher body weight and body mass index and were more likely to be obese, similar to an earlier studies (Kanjilal et al., 2008; Mattoo et al., 2011). Increasing age was also reported to be a risk factor for developing MS in general population (Deepa et al., 2007) and substance dependent populations (Mattoo et al., 2011) in India.

Significant predictors determined by simple binary logistic regression analysis were being older, higher education, greater duration of dependence, presence of physical comorbidity, higher body weight, higher body mass index. Of all the predictors, odds ratio was highest for BMI ≥25. A study from India in general population had reported similar predictors for MS: being older (10 years more than those without the syndrome), higher anthropometric parameters, and presence of CVD, hypertension and diabetes. WC and BMI were considered better predictors of MS when compared with WHR in Asian Indians (Kanjilal et al., 2008 & Grover et al., 2011).

These facts point to the need for physical examination and measurement of weight, waist circumference and blood pressure to be an essential part of the assessment of patients seeking de-addiction, especially for those aged >30 years.
This study had certain limitations. Being a hospital based sample, it was not a true representation of the community. A male only sample puts a restriction on the generalization of the findings. The lack of a healthy control group further limits the conclusions on causal links.

To conclude, MS is prevalent amongst substance dependent subjects. Older age, greater duration of dependence, presence of physical comorbidity, higher body weight, and higher body mass index are certain risk factors for development of MS. However, these findings need further validation with larger samples, prospective and longitudinal designs.

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The German Journal of Psychiatry ISSN 1433-1055 http:/www. gjpsy.uni-goettingen.de
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