Prevalence and predictors of metabolic syndrome in schizophrenia patients from Assam

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ABSTRACT

Background: Metabolic abnormalities contribute enormously to morbidity and mortality in schizophrenia. Objectives: Our objectives were to determine the (i) prevalence of metabolic syndrome (MS); and (ii) predictors for MS in schizophrenia patients from Assam. Materials and Methods: Seventy-five schizophrenia patients were evaluated for MS. Risk factors were assessed by odds ratios (ORs) with 95% confidence intervals (CIs). Results: Fifty-nine patients (78.7%) had a metabolic abnormality. Twenty-two patients (29.3%, 95% CI: 19.9%–40.8%) fulfilled the criteria for MS. Female gender (adjusted OR = 7.8, 95% CI: 1.7–36.4), smoking (adjusted OR = 7.9, 95% CI: 1.7–35.8), family history of chronic lifestyle disease (adjusted OR = 4.4, 95% CI: 1.3–15.2), and atypical antipsychotic use (adjusted OR = 4.3, 95% CI: 1.1–16.9) significantly predicted MS. Conclusion: Metabolic abnormalities exist widely in schizophrenics from Assam. Females, smokers, and those with family history of chronic diseases and using atypical antipsychotics are at greater risk.

Key words: Metabolic abnormalities, Northeast India, schizophrenia
regarded as an ethnological transition zone between the Indian sub-continent in the West and the East/Southeast Asia region in the East. Thus, data on the prevalence and risk factors for MS in schizophrenia from this population are of special interest.

With this background, we conducted this study with the primary aim of estimating the prevalence of MS in a sample of schizophrenia patients from Assam. In addition, we determined the predictors of MS in those patients.

MATERIALS AND METHODS

Study design
We conducted an analytical cross-sectional study in Gauhati Medical College and Hospital, Assam, after obtaining the Institutional Ethical Committee approval. The patients were enrolled after they voluntarily agreed to be interviewed and gave their consent.

Sample size
The prevalence of MS in schizophrenia patients from India varies from 12% to 36%. Assuming the prevalence in Assam to be 25%, we calculated the required sample size with a 95% confidence interval (CI) and 10% margin of error. On this basis, it was found that at least 73 patients would be needed.

Subjects
We recruited 75 schizophrenia patients diagnosed by experienced psychiatrists as per the International Classification of Disease-10 guidelines. Pregnant women were excluded from the study. We collected data on sociodemographic factors, lifestyle habits, family history, and antipsychotic usage in interview schedules, which were validated and pilot-tested in ten patients before initiating the actual study.

Waist circumference (WC) and blood pressure (BP) were measured using standard protocol. Fasting venous samples were collected for quantifying fasting blood glucose (FBG), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TGL) in VITROS 5600 Autoanalyzer (Ortho Clinical Diagnostics, USA) photometrically. The results were validated using third party control materials (Bio-Rad, USA and Christian Medical College, Vellore, India).

We used guidelines recommended jointly by the International Diabetic Federation, National Heart Lung and Blood Institute, World Health Federation, American Heart Association, International Atherosclerosis Society, and International Association for the Study of Obesity to identify MS. Accordingly, the presence of three or more of the following five components defined MS: Increased WC (≥90 cm for men, ≥80 cm for women); elevated TGLs (≥150 mg/dL) or drug treatment for elevated TGL; reduced HDL-C (<40 mg/dL in males, <50 mg/dL in females) or drug treatment for reduced HDL-C; elevated BP (systolic ≥130 mmHg and/or diastolic ≥85 mmHg) or antihypertensive treatment in a patient with HTN; and elevated FBG (≥100 mg/dL) or drug treatment for hyperglycemia.

Statistics
Continuous data were expressed as means with standard deviation. The proportion of MS and its individual components were summarized as count and percentage, with 95% CI. Potential risk factors between the patients with and without MS were compared, using Fischer’s exact test or Chi-square test, as applicable. The association of the risk factors with MS was estimated using odds ratios (ORs) with 95% CIs in OpenEpi version 3.0.1 (http://www.OpenEpi.com). Further, these were verified using adjusted ORs through multiple logistic regressions in SPSS version 17.0 suite (SPSS, Chicago, IL, USA). A two-tailed \( P < 0.05 \) was considered statistically significant.

RESULTS

The patient characteristics are summarized in Supplementary Table 1. The criteria for MS (≥ 3 components) were met by 22 patients (29.3%, 95% CI: 19.9–40.8%) [Supplementary Table 2]. Overall, 59 patients (78.8%, 95% CI: 72.5–82.2%) had at least one MS component. Reduced HDL-C was the most common abnormality (49.3%), followed by raised BP (45.3%), elevated TGL (36%), increased WC (22.7%), and elevated FBG (12%).

Univariate analyses revealed female gender (OR = 3.1, 95% CI: 1.1–9.4), smoking (OR = 3.2, 95% CI: 1.1–9.8), and having a family history for lifestyle diseases (OR = 3.7, 95% CI: 1.3–11.5) as significant \( (P < 0.05) \) risk factors for MS [Table 1]. Newly diagnosed and antipsychotic naive patients apparently had 50% lesser risk for MS although not significantly (OR = 0.5, 95% CI: 0.1–1.9). However, patients using atypical antipsychotics were at significantly enhanced risk (OR = 3.8, 95% CI: 1.2–11.8) for MS than patients who were drug-naïve or on typical antipsychotics.

In multivariate analysis, the female gender (adjusted OR = 7.8, 95% CI: 1.7–36.4), smoking (adjusted OR = 7.9, 95% CI: 1.7–35.8), a family history of chronic lifestyle disease (adjusted OR = 4.4, 95% CI: 1.3–15.2), and use of atypical antipsychotics (adjusted OR = 4.3, 95% CI: 1.1–16.9) persisted to be independent determinants for MS [Table 1]. Collectively, these four predictors accounted for 40% (Nagelkerke \( R^2 \) = 0.40) of the variance, with a correct prediction rate of 78.7%.

DISCUSSION

The prevalence of MS in schizophrenia varies across different ethnic groups. The criteria for MS were satisfied by
29.3% of our patients. This was similar to the findings of Bajaj et al.\textsuperscript{[6]} but higher than in South India\textsuperscript{[4]} and lower than in North India.\textsuperscript{[5]} The Indian population is heterogeneous. Differences in lifestyle and sociodemographic profile may be a reason for dissimilar prevalence of MS across different regions. Further, although MS is recognized worldwide as a distinct entity, the guidelines for identifying MS by different organizations vary. Using different guidelines in the same sample may yield considerably different estimates for MS prevalence.\textsuperscript{[14]} Hence, to avoid such ambiguities, we used the guidelines issued jointly by different international bodies to unify and harmonize the criteria for MS.\textsuperscript{[9]} Among the neighboring East/Southeast Asian nations, the proportion of MS in our patients was comparable to that in Japanese,\textsuperscript{[10]} higher than in Indonesians\textsuperscript{[11]} and remarkably lower than in Thai,\textsuperscript{[12]} and Koreans.\textsuperscript{[13]} Despite Indians having a predisposition to develop MS in general, schizophrenia patients from India have comparatively lower MS prevalence. This might be due to the lower rates of prescribing atypical antipsychotics (which is considered a major risk factor for MS) in India.\textsuperscript{[15]} In the current study also, only 42 patients (56%) used atypical antipsychotics. More than three-fourths of the patients had at least one metabolic abnormality. Reduced HDL-C and HTN are widely prevalent in Assam.\textsuperscript{[18]} Their increased prevalence in our subjects may be a reflection of the existing predisposition to these conditions in the general population. However, the frequency of increased WC and elevated FBG in our sample was substantially higher than in the general population. As opposed to nearly 7% and 1% of the general population of Assam who are overweight and diabetic,\textsuperscript{[18]} 22.7% and 12% of our schizophrenic patients had increased WC and elevated FBG, respectively.

### Table 1: Schizophrenia patients with and without metabolic syndrome

| Variable/risk factor | MS present (22 subjects), n (%) | MS absent (53 subjects), n (%) | Fischer’s exact test \((P\) value) | Crude OR (with 95% CI) | Adjusted OR (with 95% CI) |
|----------------------|---------------------------------|-------------------------------|----------------------------------|------------------------|--------------------------|
| Gender               |                                 |                               |                                  |                        |                          |
| Female               | 10 (45.5)                       | 11 (20.8)                     | 0.06                             | 3.1 (1.1-9.4)          | 7.8 (1.7-36.4)           |
| Male                 | 12 (54.5)                       | 42 (49.2)                     |                                  |                        |                          |
| Age (years)          |                                 |                               |                                  |                        |                          |
| 20-29                | 3 (13.6)                        | 5 (9.4)                       |                                  |                        |                          |
| 30-39                | 3 (13.6)                        | 6 (11.3)                      |                                  |                        |                          |
| 40-49                | 7 (31.8)                        | 20 (37.7)                     |                                  |                        |                          |
| 50-59                | 5 (22.7)                        | 11 (20.8)                     |                                  |                        |                          |
| >60                  | 4 (18.3)                        | 11 (20.8)                     |                                  |                        |                          |
| Residence            |                                 |                               |                                  |                        |                          |
| Urban                | 5 (22.7)                        | 19 (35.8)                     | 0.41                             | 0.5 (0.2-1.6)          | -                        |
| Rural                | 17 (77.3)                       | 34 (64.2)                     |                                  |                        |                          |
| Religion             |                                 |                               |                                  |                        |                          |
| Hindu                | 17 (77.3)                       | 38 (71.7)                     | 0.85                             | 1.3 (0.4-4.7)          | -                        |
| Muslim               | 5 (22.7)                        | 15 (28.3)                     |                                  |                        |                          |
| Marital status       |                                 |                               |                                  |                        |                          |
| Single               | 11 (50.0)                       | 29 (54.7)                     | 0.90                             | 0.8 (0.3-2.3)          | -                        |
| Married              | 11 (50.0)                       | 24 (45.3)                     |                                  |                        |                          |
| Employment status    |                                 |                               |                                  |                        |                          |
| Unemployed           | 10 (45.5)                       | 20 (37.7)                     | 0.71                             | 1.4 (0.5-3.8)          | -                        |
| Employed             | 12 (54.5)                       | 33 (62.3)                     |                                  |                        |                          |
| Smoking              |                                 |                               |                                  |                        |                          |
| Yes                  | 15 (68.2)                       | 21 (39.6)                     | 0.04                             | 3.2 (1.1-9.8)          | 7.9 (1.7-35.8)           |
| No                   | 7 (31.8)                        | 32 (60.4)                     |                                  |                        |                          |
| Alcohol              |                                 |                               |                                  |                        |                          |
| Yes                  | 9 (40.9)                        | 20 (37.7)                     | 0.99                             | 1.1 (0.4-3.2)          | -                        |
| No                   | 13 (59.1)                       | 33 (62.3)                     |                                  |                        |                          |
| Family history of DM/CVD/HTN |                   |                               |                                  |                        |                          |
| Yes                  | 15 (68.2)                       | 19 (35.8)                     | 0.02                             | 3.7 (1.3-11.5)         | 4.4 (1.3-15.2)           |
| No                   | 7 (31.8)                        | 34 (64.2)                     |                                  |                        |                          |
| First episode        |                                 |                               |                                  |                        |                          |
| Yes                  | 3 (13.6)                        | 13 (24.5)                     | 0.47                             | 0.5 (0.1-1.9)          | -                        |
| No                   | 19 (86.4)                       | 40 (75.5)                     |                                  |                        |                          |
| Anti-psychotic use   |                                 |                               |                                  |                        |                          |
| Anti-psychotic naïve | 3 (13.6)                        | 13 (24.5)                     | 0.47                             | 0.5 (0.1-1.9)          | -                        |
| Atypical anti-psychotic | 17 (77.3)               | 25 (47.2)                     | 0.02                             | 3.8 (1.2-11.8)         | 4.3 (1.1-16.7)           |
| Typical anti-psychotic | 2 (9.1)                   | 15 (28.3)                     |                                  |                        |                          |

\textsuperscript{[1]} Age-wise distribution of MS was compared by Chi-square test. Except age, all the other variables were compared by the Fischer’s exact test. MS – Metabolic syndrome; OR – Odds ratio; CI – Confidence interval; df – Degrees of freedom; DM – Diabetes mellitus; CVD – Cardiovascular disease; HTN – Hypertension
In the risk factor assessment, female patients exhibited greater risk of developing MS. This is in agreement with the previous studies. [11, 19] Besides, a positive history for chronic noncommunicable diseases in the family resulted in nearly 4.5 times greater odds of developing MS. Among the modifiable risk factors, smoking, which is a known risk factor for cardiometabolic derangements, greatly enhanced the risk for MS in our patients. Moreover, use of atypical antipsychotics produced about four times greater likelihood for developing MS. This is of concern because atypical antipsychotics are the first-choice medications for schizophrenia. Previously, schizophrenics on atypical antipsychotics were found to be more susceptible for MS than those who were drug-naïve or on typical antipsychotics. [6, 19] These risk factors for MS notwithstanding, it is believed that schizophrenia itself can independently predispose to MS, possibly by altering insulin sensitivity and glucose homeostasis. [3]

Our study had limitations such as cross-sectional nature (that precluded identifying temporal relationship between schizophrenia and the metabolic abnormalities) and lack of reliable information on duration of antipsychotic use in patients using medication.

CONCLUSION

We described MS and its components in schizophrenia patients from Assam for the first time. We also identified the important risk factors for MS in these patients. Schizophrenia patients often receive inadequate medical care and low rates of treatment for co-morbidities like HTN, DM, dyslipidemia and obesity. [20] Health-care providers should be trained and sensitized for monitoring schizophrenic patients for metabolic derangements. Methods to tackle MS and the responsible risk factors should be incorporated as part of the detailed workup and management protocol for schizophrenia.

Acknowledgment

We gratefully acknowledge the immense help provided by the psychiatrists and other staff from the Department of Psychiatry, Gauhati Medical College and Hospital in the course of the study. We are especially thankful to Dr. Shyamanta Das, Assistant Professor, Department of Psychiatry, Gauhati Medical College and Hospital for his valuable suggestions and constant motivation. We are indebted to Dr. Dipesh Bhagawati, Professor, Department of Psychiatry, Gauhati Medical College and Hospital for facilitating the smooth conduct of the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Brown S. Excess mortality of schizophrenia. A meta-analysis. Br J Psychiatry 1997;171:502-8.
2. Lan YL, Chen TL. Prevalence of high blood pressure and its relationship with body weight factors among inpatients with schizophrenia in Taiwan. Asian Nurs Res (Korean Soc Nurs Sci) 2012;6:13-8.
3. Braceland FJ, Meduna LD, Vaihulis JA. Delayed action of insulin in schizophrenia. Am J Psychiatry 1945;102:108-10.
4. Kumar CN, Thirthalli J, Suresha KK, Arunachala U, Gangadhar BN. Metabolic syndrome among schizophrenia patients: Study from a rural community of South India. Asian J Psychiatr 2013;6:532-6.
5. Grover S, Nebhianini N, Chakrabarti S, Avasthi A, Basu D, Kulhara P, et al. Cardiac risk factors and metabolic syndrome in patients with schizophrenia admitted to a general hospital psychiatric unit. Indian J Psychiatry 2014;56:371-6.
6. Bajaj S, Varma A, Srivastava A, Verma AK. Association of metabolic syndrome with schizophrenia. Indian J Endocrinol Metab 2013;17:890-5.
7. International Institute for Population Sciences (IIPS), World Health Organization, World Health Organization-India-WR Office. Ch. 5. Morbidity prevalence. In: Health System Performance Assessment - World Health Survey 2003 India; 2006. p. 53-70. Available from: http://www.who.int/healthinfo/survey/whs_hispa_book.pdf. [Last accessed on 2017 Mar 18].
8. Ali AN, Das I. Tribal situation in Northeast India. Stud Tribals Tribals 2003;1:141-8.
9. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640-5.
10. Sugawara N, Yasui-Furukori N, Sato Y, Umeda T, Kishida I, Yamashita H, et al. Prevalence of metabolic syndrome among patients with schizophrenia in Japan. Schizophr Res 2010;123:244-50.
11. Marthoenis M, Aichberger MC, Puteh I, Syahrial S, Schouler-Ocak M. Metabolic syndrome among psychiatric inpatients with schizophrenia in Indonesia. Asian J Psychiatr 2015;15:10-4.
12. Suttajit S, Pilakanta S. Prevalence of metabolic syndrome and its association with depression in patients with schizophrenia. Neuropsychiatr Dis Treat 2013;9:941-6.
13. Kang SH, Kim KH, Kang GY, Lee KH, Kim KK, Soh M, et al. Cross-sectional prevalence of metabolic syndrome in Korean patients with schizophrenia. Schizophr Res 2011;128:179-81.
14. John AP, Koloth R, Dragovic M, Lim SC. Prevalence of metabolic syndrome among Australians with severe mental illness. Med J Aust 2009;190:176-9.
15. Papastasiou E. The prevalence and mechanisms of metabolic syndrome in schizophrenia: A review. Ther Adv Psychopharmacol 2013;3:33-51.
16. Bora K, Pathak MS, Borah P, Das D. Variation in lipid profile across different patterns of obesity – Observations from Guwahati, Assam. J Clin Diagn Res 2015;9:OC17-21.
17. National Cardiovascular Disease Database. Ministry of Health and Family Welfare Government of India and World Health Organization. Available from: http://www.searo.who.int/india/topics/cardiovascular_diseases/NCD_Resources_National_CVD_database-Final_Report.pdf?ua=1. [Last accessed on 2017 Mar 18].
18. International Institute for Population Sciences (IIPS), Macro International. National Family Health Survey (NFHS-3), India, 2005-2006. Assam. Mumbai: IIPS; 2008.
19. De Hert M, Schorens V, Sweerts K, Van Eyck J, Hanssens L, Sinco S, et al. Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: A retrospective chart review. Schizophr Res 2008;101:295-303.
20. Nasrallah HA, Meyer JM, Goft DC, McEvoy JP, Davis SM, Stroup TS, et al. Low rates of treatment for hypertension, dyslipidemia and diabetes in schizophrenia: Data from the CATIE schizophrenia trial sample at baseline. Schizophr Res 2006;86:15-22.
### Supplementary Table 1: Sociodemographic profile, clinical variables, and background information

| Variable                                      | Values as mean±SD, n (%)                     |
|-----------------------------------------------|----------------------------------------------|
| Age (years)                                   | 43.04±9.75                                   |
| Sex                                           |                                              |
| Male                                          | 54 (72.0)                                    |
| Residence                                     |                                              |
| Rural                                         | 51 (68.0)                                    |
| Religion                                      |                                              |
| Hindu                                         | 55 (73.3)                                    |
| Muslim                                        | 20 (26.7)                                    |
| Marital status                                |                                              |
| Currently single                              | 40 (53.3)                                    |
| Currently on paid employment                  |                                              |
| Yes                                           | 45 (60.0)                                    |
| Family history of DM/HTN/CVD                  |                                              |
| Yes                                           | 34 (45.3)                                    |
| Food habit                                    |                                              |
| Nonvegetarian                                 | 75 (100.0)                                   |
| Smoking habit                                 |                                              |
| Yes                                           | 36 (48.0)                                    |
| Alcohol consumption                           |                                              |
| Yes                                           | 29 (38.7)                                    |
| Whether first episode (newly diagnosed)       |                                              |
| First episode (newly diagnosed)               | 16 (21.3)                                    |
| Previously diagnosed                          | 59 (78.7)                                    |
| Medication use                                |                                              |
| Anti-psychotic naive (untreated)              | 16 (21.3)                                    |
| Typical anti-psychotic                        | 17 (22.7)                                    |
| Atypical anti-psychotic                       | 42 (56.0)                                    |
| Systolic BP (mmHg)/diastolic BP (mmHg)        | 158±30.5/101.4±11.75                         |
| WC (cm)                                       | 109.6±12.2                                   |
| TGL (mg/dL)                                   | 176.4±55.8                                   |
| HDL-C (mg/dL)                                 | 35.16±8.12                                   |
| FBG (mg/dL)                                   | 138.8±19.24                                  |

SD – Standard deviation; DM – Diabetes mellitus; HTN – Hypertension; CVD – Cardiovascular disease; BP – Blood pressure; WC – Waist circumference; TGL – Triglyceride; HDL-C – High-density lipoprotein cholesterol; FBG – Fasting blood glucose

### Supplementary Table 2: Distribution of metabolic abnormalities in the study subjects (n=75)

| n    | Percentage (95% CI) |
|------|---------------------|
| One  | 24                  | 32.0 (22.4-43.6) |
| Two  | 13                  | 17.3 (9.9-27.9)  |
| Three| 16                  | 21.3 (13.3-32.3) |
| Four | 4                   | 6.7 (4.5-10.6)   |
| Five | 2                   | 1.4 (0.1-9.9)    |
| None | 16                  | 21.3 (13.3-32.3) |
| At least one abnormality                     | 59                  | 78.7 (72.5-82.2) |
| Metabolic syndrome (≥3 abnormalities)        | 22                  | 29.3 (19.9-40.8) |

WC – Waist circumference; TGL – Triglyceride; HDL-C – High-density lipoprotein cholesterol; BP – Blood pressure; FBG – Fasting blood glucose; CI – Confidence interval