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Factors Affecting the Management of Somatic Comorbidity in Tunisian Patients with Schizophrenia

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Abstract

Schizophrenia is often accompanied by somatic comorbidities, which make the management challenge of such patients more difficult. In this study, we proposed to identify the sociodemographic and clinical factors correlating with somatic comorbidities in patients with schizophrenia to facilitate screening and prevention. It was a retrospective descriptive study of 78 schizophrenia patients in clinical remission and followed in outpatient psychiatry. In addition to the acquired records, other data were provided by the clinical and biological examinations performed for each patient. The evaluation of the therapeutic adherence was carried out using the Drug Attitude Inventory (DAI).Seventy-six patients (97.4%) had somatic comorbidities with a mean of 3.83 (± 1.81). This number increased significantly in males, older patients, couples, urban patients, and those receiving a combination therapy. According to a multivariate study, the four predictors of an increased risk of comorbidities were age, use of psychoactive substances, waist size and therapeutic adherence.Our findings focus on somatic comorbidities risk in schizophrenia patients, requiring particular vigilance in their follow-up, and suggest some modifiable clinical factors that might be a preferred target for reducing or preventing the occurrence of such disorders.

Keywords Schizophrenia · Comorbidity · Somatic · Risk factors

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Introduction

Schizophrenia is a major psychotic disorder which represents a substantial burden for patients. This burden is still made heavier by the high prevalence of somatic comorbidities [1]. Combining schizophrenia and physical illnesses complicates the care of these patients and affects their life expectancies; mainly because of the cardiovascular risk they may face [2].

Schizophrenia itself and the unhealthy lifestyle habits, the addictive behavior [3] and the side effects of antipsychotics (AP) [4] are associated with dyslipidemia, hyperglycemia, and overweight contributing to the overall risk of developing somatic diseases including the metabolic syndrome and cardiovascular disease. Given the magnitude of this public health problem and the predictable character of many of these comorbidities, some recommendations that require regular and codified clinical and biological monitoring, were elaborated [5]. Unfortunately, there are many difficulties to the recognition and management of physical illnesses in patients suffering from schizophrenia. In Tunisia, schizophrenic patients and their parents are rather reluctant to different explorations and adhere very little to the proposed international monotoring protocols. In addition, we have neither national screening strategies, nor the required means to ensure an optimum monitoring. Such strategies could improve these patients' life expectancy and morbidity figures [6].

The objective of this study was to identify the sociodemographic and clinical correlated factors with somatic comorbidity in patients with schizophrenia followed in the outpatient psychiatriy department in Sfax, Tunisia, to facilitate their detection and if possible their prevention.

Methods

Participants

This descriptive and retrospective study took place from January 2016 to June 2016. We recruited all the patients who were diagnosed with schizophrenia or schizoaffective disorder according to the Diagnostic and Statistical Manual of Mental Disorders (fourth edition-text revision: DSM-IV-TR), and who were followed in the outpatient psychiatriy department at Hedi Chaker university hospital in Sfax, Tunisia.

The following inclusion criteria were applied:

– Diagnosis of schizophrenia or schizoaffective disorder according to the DSM-IV-TR;
– Patients in clinical remission at the time of the study;
– Age ranging from 20 to 65 years;
– Written informed consent obtained before participation in the study;
– Willing and able to participate in the study.

A total of seventy-eight patients were screened. The purpose, steps, and methods of this study were shared with the participants and each one provided written informed consent before the interviews.

Procedure

First, eligible patients were screened for schizophrenia or schizoaffective disorder by two independent and experienced psychiatrists. The clinical interview was based on the DSM-IV-TR criteria. The clinical interview also included questions about mental illness, treatment side effects, substance consumption and medical history.

For the study requirements, patients completed a questionnaire covering demographic characteristics including age, gender, residence area, civil status, educational level and socio-economic standard. We checked the inpatient and outpatient medical records of the patients to obtain mental illness-related data.

Then, the patients underwent measurements of weight, height, and waist circumference.

We performed a complete physical examination, an electrocardiogram (ECG) and laboratory tests including a metabolic balance, an infectious balance, hepatitis and HIV serology, blood count, erythrocyte sedimentation rate, C-reactive protein and a lipid profile for each of them. To search for the treatment biological side effects, we performed liver function tests and a prolactin test. The evaluation of the therapeutic adherence was performed using the drug attitude inventory (The Drug Attitude Inventory (DAI-10)) [7].

Ethical Considerations

The research complied with all ethical guidelines. Patients were previously informed of the study objectives and consent was obtained from all of them before they were enrolled in the study.

Statistical Analysis

Data collection and analysis were performed using the 20th version of Statistical Package for Social Sciences (SPSS) computer software. Descriptive statistics were presented in frequency, percentage, mean, standard deviation, and minimum – maximum. Chi-square test or Fisher exact test was used to test possible differences between groups in terms of categorical variables. Student's t-test was utilized for comparing the continuous variables. Pearson's correlation coefficient "r" was used to measure two quantitative variables association. A hierarchical logistic regression was conducted to determine the predictive power of different variables that were likely to be associated with somatic comorbidities. The significance level was set to 5% for all the tests.

Table 1 Prevalence of somatic comorbidities in schizophrenia

Pathologies	Number	Percentage (%)
Diabetes	7	9
Overweight/ obesity	36	46.2
Dyslipidemia	7	9
Heart diseases	59	75.64
Metabolic syndrome	5	6.4
Bone pathologies	35	44.87
Respiratory pathologies	36	46.2
Sexual dysfunction	28	35.89

Table 2 Clinical and demographic factors correlated with the number of somatic comorbidities

Variables	p value
Age	p = 0.001; r = 0.36
Male gender	p = 0.007
urban areas	p = 0.02
Unemployed status	p = 0.05
Weight	P = 0.016; r = 0.272
Waist circumference	p = 0.005; r = 0.318
Consumption of psychoactive substances	p = 0.000

Results

Descriptive Study

The sex ratio (male / female) was 3.33. The patients' average age was 41.78 years (± 11.56 years) with extremes of 21 and 65 years. Their socioeconomic standard was low for 85.9% of the patients. Among the patients, 38.5% lived in rural areas and 25.6% received insufficient family support.

Twenty-four patients (30.8%) had a medical record history and 22 (28.2%) had a surgical one. Fifty-six patients (71.8%) consumed psychoactive substances. More than two-thirds (67.9%) of patients consumed tobacco, 19.2% consumed two psychoactive substances and 14.1% consumed at least three psychoactive substances.

Twenty-eight patients (35.9%) declared they consumed alcoholic beverages with an average of four beers per day. Five patients (6.4%) admitted using cannabis and one using heroin. The use of solvents, such as glue and diluents, was reported in three patients (3.8%). As for drug abuse, only one patient was addicted to morphine and two were used to trihexyphénidyle. Twenty patients (35.1%) had initiated the above mentioned substances consumption after being diagnosed with schizophrenia.

All patients were in combination therapy with an average of 4.47 medications. First generation AP was prescribed for 92.3% of the patients. A regular follow up was registered for 51% of the patients. The side effects of the most commonly used treatments were respectively psychological (drowsiness, anxiety ...) for 98.7%, adrenolytic (sedation, hypotension ...) for 92.3%, anticholinergic (dry mouth, constipation ...) for 89.7% and neurological (parkinsonism, late dyskinesia...) for 87.1%. According to the DAI-10, 83.3% of patients had good compliance.

Seventy-six patients (97.4%) had somatic comorbidities; two patients (2.6%) were comorbidity free. The comorbidities maximum number was eight, with an average of 3.83 (± 1.81).

Table 3 Results of logistic regression with number of comorbidities as dependent variable and demographic and clinical variables as predictors

	Beta Coefficient	p value
Age	0.291	0.002
Consumption of psychoactive substances	0.509	0.000
Waist circumference	0.241	0.010
Drug adherence	0.205	0.026

Seven of our patients (9%) had diabetes. The diagnosis for diabetes was retained after an interval of 5 to 30 years after being diagnosed with schizophrenia, an average of 19.85 years (± 10.60). Four patients had degenerative complications (5.1%) of a neuropathy diabetic type leading to limb amputation (two patients) and nephropathy diabetic (one patient). This same patient had both retinopathy and neuropathy diabetic.

At the time of the survey, the patients' average weight was 73.25 kg (± 15.89 kg). Body mass index (BMI) was calculated following the standard formula of the ratio between weight (in kg) and squared height (in m). BMI categories were underweight (BMI < 18.5), normal (BMI = 18.5–24.9), overweight (BMI = 25–29.9), and obese (BMI ≥30). Among our patients, 46.2% were either overweight or obese. The patients' waist circumference varied from 74 cm to 131 cm with an average of 101.10 cm (± 11.44 cm).

In our study sample, 41 patients (52.6%) were sedentary, 17 (21.8%) were malnourished, 38 (48.7%) had a diet rich in fat, 42 (53.8%) excessively consumed sweety products (white sugar, soft drinks, tea, coffee ...) and only six (7.7%) had regular physical activity.

Seven patients (9%) had dyslipidemia (3.8% had hypertriglyceridemia and 6.4% suffered from hypercholesterolemia).In all our cases, the diagnosis was performed after being diagnosed with schizophrenia. The diagnosis delay ranged from one to thirty years, with an average of 17.71 years (± 12.27 years).

Heart diseases were reported for 59 patients (75.6%). The diagnosis was performed before initiating the psychotropic treatment for four patients (6.7%). For the rest (93.2%), the diagnosis was carried out after the initiation of the treatment. Five of our patients (6.4%) had metabolic syndrome defined according to the International Diabetes Federation (IDF) criteria. A proportion of 46.2% of our patients were diagnosed with respiratory pathologies (44.9% had obstructive bronchopneumopathies and 1.3% had tuberculosis).

Thirty five patients (44.8%) were diagnosed with bone pathologies: 82.8% had fractures and 2.8% had osteoporosis. These pathologies occurred before the initiation of the treatment for 12 patients (34.3%) and after the beginning of the treatment for the remaining 23 patients (65.7%). Sexual dysfunction (erectile dysfunction, abnormal orgasm, premature ejaculation and frigidity) were found in 28 patients (35.8%). Among them, 96.4% reported that these dysfunctions occurred after the initiation of the therapy. (Table 1)

Analatycal Study

The older the patient, the greater the number of somatic comorbidities ($p = 0.001$; $r = 0.36$). In fact, with age, the patients were more likely to have diabetes (56 years versus 40.38 years; $p = 0.000$), dyslipidemia (57.28 years versus 40.25 years; p = 0.00), more respiratory diseases (44.69 years versus 39.28 years; $p = 0.038$), sexual dysfunctions (46.10 years versus 39.32 years; $p = 0.012$) and metabolic syndrome (56.20 years versus 40.79 years; $p = 0.003$). Besides, they had a larger waist circumference meaning a more important abdominal obesity ($p = 0.025$).

The male subjects were more likely to develop somatic comorbidities (100% versus 88.9%; $p = 0.051$). The male gender correlated with a larger number of comorbidities (4.13 versus 2.83; $p = 0.007$). The male gender also correlated with psychoactive substances consumption ($p = 0.000$) and the occurrence of respiratory diseases (60% versus 0%; p = 0.000). Some somatic disorders were more common in male subjects without being correlated with, namely,

bone diseases (50.8% versus 27.8%; $p = 0.108$) and sexual dysfunctions (37.3% versus 33.3%; $p = 1$). As for women, they suffered more from metabolic syndrome (16.7% versus 3.3%; $p = 0.078$), diabetes (11.1% versus 8.3%; $p = 0.659$) and dyslipidemia (16.7% versus 6.7%; $p = 0.343$). Women were also more obese (66.7% versus 40%; $p = 0.061$). Interestingly, there were no correlations among these comorbidities.

There was no statistically significant relationship between low socioeconomic standards and somatic comorbidities ($p = 0.264$ and 0.701 respectively). Neither did a low educational level correlate significantly with such comorbidities ($p = 0.51$ and 0.402, respectively). Being married, however, correlated with a greater number of these comorbidities (5 versus 3.2; $p = 0.00$). They were closely related with bone diseases, sexual dysfunction and psychoactive substances consumption ($p = 0.029$, 0.000 and 0.027 respectively). Living in urban areas correlated with a greater number of comorbidities (4.2 versus 3.1; $p = 0.02$). Diabetes was the most highly correlated comorbidity with residing in cities (14.6% versus 0%; $p = 0.039$). The unemployed schizophrenic subjects had more comorbidities than their professionally active conterparts (4.5 versus 3.6; $p = 0.05$). Indeed, they were more likely to suffer frome sexual dysfunctions ($p = 0.031$) and smoking addiction ($p = 0.024$).

An unbalanced diet, excessively rich in calories (high in fat and sweets, but low in fibers, vegetables and fruit), correlated with overweight ($p = 0.000$) and high blood pressure ($p = 0.027$). As for an irregular physical activity, it did not significantly correlate with any somatic comorbidity. The more the weight increases, as well as the waist circumference, the greater the number of somatic comorbidities is (respectively $p = 0.016$; $r = 0.272$ and $p = 0.005$; $r = 0.318$). Dyslipidemia and hypertension were the only comorbidities to be closely linked with a BMI synonym of overweight or obesity (respectively 29.54 versus 24.71; $p = 0.025$ and 28.96 versus 24.31; $p = 0.003$).

On the other hand, as the follow-up period was shorter, the occurrence of somatic comorbidities was more significant (18 versus 35; $p = 0.03$).

Psychoactive substances consumption correlated with a significant number of somatic comorbidities ($p = 0.000$). Psychoactive substances consumers among our patients had more respiratory diseases ($p = 0.000$), more bone diseases ($p = 0.048$) and more obesity-related pathologies ($p = 0.012$). Smoking was associated with the development of heart diseases ($p = 0.001$), obesity ($p = 0.02$) and respiratory pathologies ($p = 0.003$). The greater the number of cigarettes consumed per year, the more important the number of comorbidities. (Table 2)

A poor adherence to a therapeutic follow-up did not correlate with the prevalence of somatic comorbidities ($p = 1.00$). The older subjects were more medically adherant than the young ($p = 0.033$; $r = 0.241$). Subjects with good therapeutic adherence had more sexual dysfunctions ($p = 0.007$), dyslipidemia ($p = 0.000$) diabetes ($p = 0.000$), hypertension ($p = 0.032$) and metabolic syndrome ($p = 0.008$). Concerning the combination therapy, it was associated with a greater number of somatic comorbidities ($p = 0.061$; $r = 0.213$). The treatment with two or more AP correlated with hypertension ($p = 0.019$). There was no significant correlation between AP (first or second generation) used for neurological or endocrinian side effects ($p = 0.131$ and 1, respectively).

The multivariate analysis via the multiple linear regression showed that four factors were strongly associated with the rise of the number of comorbidities such as age, use of psychoactive substances, waist circumference and treatment adherence. The adjusted R-square was estimated at 41.4%. (Table 3)

Discussion

Comorbidities Prevalence

In our study, the somatic comorbidity was found in almost all the patients (97.4%). Data on the prevalence of somatic pathologies among people with schizophrenic disorders are relatively rare since these patients are usually excluded from studies on somatic diseases. Furthermore, those with somatic comorbidities are also excluded from psychiatric investigations. However, it is now well established that schizophrenic subjects exhibit high somatic comorbidity rates [8, 9]. Different studies have shown that 40 to 80% of schizophrenic patients have associated somatic diseases [10–12]. Paradoxically, all the entire literature confirms the absence of screening and the underestimation of these diseases among schizophrenic patients [13, 14]. According to some studies, 45 to 53% of physical comorbidities are not diagnosed and therefore not treated [15, 16] allowing them to evolve to an advanced stage [12]. Routine screening examinations to patients on admission would enable the detection of 90% of such diseases [17, 18].

Correlated Factors to the Existence of Comorbidities

The multivariate analysis by multiple linear regression showed that four factors were strongly associated with a rise in the number of comorbidities namely age, psychoactive substances consumption, waist circumference and treatment compliance.

Age

Acording to various studies [10, 19], the prevalence and severity of somatic comorbidities increase with age. This finding was confirmed in our study where the prevalence of comorbidities increased with age ($p = 0.001$; $r = 0.36$). The older the subject was, the more somatic comorbidities he presented ($p = 0.002$).

Psychoactive Substances Consumption

Fifty-six patients (71.8%) among our study sample used psychoactive substances. This percentage is significantly higher than those reported in various previous studies [20, 21]. This might be explained by the predominance of men, heavy tobacco users, in our sample.

In addition, 35.9% of our subjects consumed alcoholic beverages occasionally. This rate could be far below the real one. The consumption of this type of psychoactive substances, subject to a moral and religious disapproval in our sociocultural environment, is not always readily reported. In the occidental countries, however, alcohol abuse with or without dependence is a common feature among schizophrenic patients, and even more common than in the general population [22]. The rate of alcoholism, in patients with schizophrenia, varies from 30 to 50% across the studies [23].

As for smoking, it was noted in 67.9% of our patients. This percentage is close to those reported in the literature (74–92%) [24, 25]. Active smoking increases by 3 times the risk of coronary heart diseases [26]. It also represents a major risk factor for respiratory pathologies, strokes and neoplasias (lung cancer, head and neck, bladder ...). These facts are in line with the

results of our study, where the psychoactive substances consumption strongly correlated with a significant number of somatic comorbidities ($p = 0.000$). In fact, consumers had more respiratory diseases (p = 0.000), bone diseases ($p = 0.048$) and obesity ($p = 0.012$). Eventually, the mortality rate due to tobacco consumption was significantly higher in subjects with schizophrenia than in the general population [27].

Waist Circumference

In our study, waist circumference was a predictor of somatic comorbidities occurrence. Moreover, overweight or obese patients were at a higher risk to suffer from dyslipidemia ($p = 0.025$) and hypertension ($p = 0.003$). Most authors [28, 29] highlight the poor nutritional quality of the schizophrenic patients' diet. These patients consume few fruits and vegetables, which are the major sources of fibers, vitamins and other substances that can limit the occurrence of somatic diseases. Moreover, schizophrenic patients reduce their carbohydrates or complex carbohydrates intake in favor of saturated fat [30, 31]. The consumption of simple sugars (chocolate bars, candees ...) is not an exception as the amount of ingested sugar is higher among schizophrenic patients than control subjects [32]. The schizophrenic quantitative lipids intake is totally unbalanced. The patients' diet is too rich in saturated fatty acids and low in omega3-type fatty acid. This type of distribution of fat intake is a risk factor for cardiovascular diseases [33, 34]. These results were found in our sample population where 38 patients (48.7%) had a high fat diet and 42 (53.8%), excessively consumed sweet products (white sugar, soft drinks, tea and coffee ...). Such an unbalanced diet correlated with overweight ($p = 0.000$) and hypertension ($p = 0.027$).

Regarding physical activity, 41 patients (52.6%) in our series were sedentary. Some studies [35, 36] reported even higher rates, where around 70% of the patients with schizophrenia were sedentary, practicing no physical activities. This physical inactivity could be attributed to the sedative effects of the psychotropic treatments, which lead to the sedentary lifestyle of schizophrenic patients [37]. Although the relationship between an irregular physical activity and somatic comorbidtés was not significant in our study population, it is well known that physical inactivity plays an important role in the genesis of various somatic diseases; it is a modifiable risk factor for cardiovascular diseases [38], osteoporosis [39] and sexual dysfunctions [40].

Compliance to Drug Treatment

Among our study group members, 51% had a regular follow-up and 83.3% were good compliants. These figures deviate from the published data according to which the range of non-compliance rate in people with schizophrenic disorders varies between 11 and 90%, depending on the selected criteria [41]. Using the DAI-10, it was revealed that a self-assessment carried out by the schizophrenic, with a possible overestimation of his medication adherence may explain this result. Our study subjects who adhered well to the prescribed therapy had more somatic comorbidities. Indeed, compliance was tightly linked to the number of somatic comorbidities ($p = 0.026$). Furthermore, the combination therapy also did correlate with somatic comorbidities ($p = 0.061$). These subjects had more sexual dysfunctions ($p = 0.007$), dyslipidemia ($p = 0.000$) diabetes ($p = 0.000$), hypertension ($p = 0.032$) and metabolic syndrome ($p = 0.008$). AP drugs are known to

generate hormonal dysregulation, and sexual dysfunction, among others [42]. In the long run, they also induce basic metabolism disruptions resulting in diabetes, dyslipidemia, hypertension and consequently metabolic syndrome [43].

Limitations of the Study

The present findings must be interpreted with caution due to the limitations of the study. First, our work is known as a transversal study. This type of study, relatively easy to achieve, is a short investigation that does not allow a longitudinal view of the rate of the physical comorbidities occuring in schizophrenic patients. Second, our study population consisted of 78 schizophrenic patients. This limited number could explain the lack of correlations between the various modifiable risk factors and the somatic comorbidities. The refusal of many patients to take part in the study is at the origin of the sample small size.

Conclusion

Despite the limitations of the present study, the results showed that some sociodemographic and clinical factors could affect the management of physical health in schizophrenia. By addressing the main risk factors of somatic comorbidities in schizophrenic patients, we would like to forward these recommendations aimed at the optimization of care for such a population. The psychiatrist plays an important role in improving the short and long run schizophrenic subjects' physical health. He/She is required to provide medical monitoring to these patients, optimize screening and primary prevention of possible comorbid somatic diseases and ensure appropriate treatment if necessary. They should, therefore, be extremely alert to patients of advanced age through more frequent clinical and laboratory monitoring. They also ought to limit the number of prescribed psychotropic drugs and avoid as much as possible the combination therapy. Failing to monitor all the constants according to the international recommendations, a targeted action on certain factors would allow the detection of possible comorbidities on time or even prevent them, limiting the damage induced on these patients' health.

In the light of our results, the modifiable factors seem to be a prime target to reduce or prevent the onset of somatic comorbidity in schizophrenic patients. These factors include the use of psychoactive substances, the waist circumference and treatment adherence. To this end, healthcare professionals should make efforts to act on these risk factors by implementing an approach that supports substance use cessation or reduction. They shoul also recommend a regular physical activity and a healthy lifestyle and diet. A systematic weighing with calculation of BMI of the patient as well as a dietary correction are needed during any clinical examination. It would also be wise to combine a motivational interviewing with the psychiatric one in case of psychoactive substances consumption and propose a substitution treatment if the patient wishes. In terms of biological monitoring, it varies depending on the prescribed AP type. However, in case of lack of compliance of patients and their families to paraclinical examinations, it would be appropriate to resort to the clinical examination whenever it is required. This screening task could be achieved in collaboration with family physicians whose role is essential and has to be promoted.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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