Research Article Volume 4, Issue 1

Hyperglycemia and FEP: Does Migration Status Matter?

Gianmarco Iuzzolino[2], Giuseppe D'Andrea[2*], Tiziano De Matteis[2], Lorenzo Guidi[1], Domenico Berardi[2], Ilaria Tarricone[1,3]

[1]Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy

[2]Department of Biomedical and NeuroMotor Sciences (DIBINEM), University of Bologna, Bologna, Italy

[3]Department of Mental Health, AUSL Bologna, Bologna, Italy

[*]**Corresponding Author:** Dr. Giuseppe D'Andrea, Giuseppe D'Andrea, Department of Biomedical and NeuroMotor Sciences (DIBINEM), University of Bologna, Bologna, Italy, University of Bologna, Via Ugo Foscolo 7, 40123, Bologna, Italy, Tel: +39 348 4679232; E-mail: giuseppe.dandrea6@studio.unibo.it

Received: 18 December 2019; **Accepted:** 02 January 2020; **Published:** 15 January 2020

Abstract

Background: Several evidence have shown hyperglycemia and diabetes are frequent in patients with psychoses. There are evidences that some ethnic minorities are at higher risk of psychosis. It is less clear if migration history is a risk factor for diabetes and hyperglycemia during first-episode psychosis (FEP). The present study aims to evaluate if migration history might influence fasting plasma glucose change during antipsychotic treatment (APs) in (FEP).

Materials and Methods: We carried out a retrospective follow-up of all FEP drug naïve patients at their first contact with Bologna West Community Mental Health Centres from January 2010 to December 2015. Blood tests carried out during the follow-up period were collated from clinical charts to evaluate the baseline fasting plasma glucose level upon starting APs treatment and at the time of follow-up. Out of 50 patients who had FEP during the recruitment period and consented to take part in the study, 25 cases had blood test results available at follow-up. We performed linear multivariate regression analysis to adjust the association between migrant status and fasting plasma glucose level of follow-up by gender, age, education, employment, APs treatment and dose.

Results: At baseline, the mean fasting plasma glucose level was within the normal range and at follow-up we observed a significant increase in the mean fasting plasma glucose in migrants. Upon multivariate linear regression analysis, migration history remained significantly associated with the follow-up fasting plasma glucose level.

Conclusions: In conclusion, we found that migrants with FEP are particularly at risk of developing hyperglycemia and type II diabetes during APs treatment.

Keywords: Antipsychotic agents; Side effects; Diabetes; Hyperglycemia; Migration; Follow up; First-episode psychosis

1. Introduction

Migrant patients are at higher risk of developing hyperglycemia and diabetes than natives (Marchesini et al. 2014; Oldroyd et al. 2005). Several risk factors have been hypothesized to be involved, including changes in life style. Moving from a frugal nutrition to a hypercaloric one (so- called pattern four transition) and reducing the amount of physical activity (Misra and Ganda 2007) are considered prime reasons. Moreover, urbanization (Katchunga et al. 2012), psychophysical stress, low socio-economic status and poor access to the national health system (Lanting et al. 2005) contribute to increase the risk of developing hyperglycemia and diabetes. Among the general population, the prevalence of diabetes is higher in men than women (Menke et al. 2015). However, the female gender has a higher risk of developing type II diabetes in certain conditions, such as low socio-economic status (Rivera et al. 2015), psycho-social stress factors or work-related ones (Heraclides et al. 2012; Krajnak 2014), and an unhealthy life style (hypercaloric diet and low physical activity) (Hare-Bruun et al. 2006).

The risk of developing diabetes is also higher (2 to 5 times) among people suffering from psychotic disorders (Ward and Druss, 2015). One possible explanation is linked to risk factors similar to those previously reported for migrants, such as unhealthy life style and low socio-economic status (Mamakou et al. 2018). In addition, patients suffering from psychotic disorders have specific risk factors that might have additive or even synergistic effects: many evidences point to both psychotic disorders and diabetes sharing a similar genetic susceptibility (Mamakou et al. 2018). Antipsychotic medications (APs) have been associated with an increased risk of developing metabolic side effects, including hyperglycemia and Type II diabetes. Such medications seem to contribute both indirectly, through weight gain, or directly, by promoting insulin resistance (Correll et al. 2015, Scheen and De Hert 2007). There are specific subpopulations of individuals at higher risk of developing diabetes during treatment with APs medications. African-American and Hispanic ethnicity seems to be associated with an increased prevalence of diabetes in both patients with psychosis and the general population (Dixon et al. 2000). Other studies support these results (Voruganti et al. 2007), and also report that European ethnicity is associated with a decreased risk of developing diabetes. What is less clear is the relation between APs treatment and Hyperglycemia in migrants.

Our study aimed to evaluate the glycaemia changes of an incidence sample of first episode psychosis patients in Bologna West (Northern Italy). We especially aimed to evaluate the impact of migration history on the risk of developing hyperglycemia during Aps treatment in FEP patients.

2. Materials and Methods

2.1 Participants

This study is part of the Bologna West First Episode Psychosis project (Bo-FEP). As described in our previous work (Tarricone et al. 2012), Bo-FEP is a naturalistic incidence study that included all patients between 18 and 64 years, drug naïve upon FEP, who had a contact with one of the three Community Mental Health Centres (CMHCs) of the West Bologna area (CMHC "Nani", "Tiarini" and "Scalo"). The inclusion period for the current study was from January 2010 to December 2015. The first episode psychosis was defined, according to APA 2004 criteria, as presence of delusions and/or hallucinations and/or disorganized speech and/or excited and/or catatonic behaviour. The diagnosis was defined according to International Statistical Classification of Disease and Related Health Problems, Tenth Revision (ICD-10) criteria. The following exclusion criteria were applied: I) patients with previous contacts with mental health services or a history of previous antipsychotic treatment; II) evidence of psychotic disorders due to organic causes or acute intoxications.

2.2 Study design

We carried out a retrospective follow-up in November 2016 of all FEP drug naïve patients at their first contact with BoWest CMHC from January 2010 to December 2015. The sociodemographic and clinical characteristics (psychiatric diagnoses, duration of untreated psychosis [DUP], kind of APs and other pharmacological treatment) were evaluated from the clinical charts and from the local computerized information system (SIT) and discussed with the clinicians responsible for the patients. The diagnoses were coded with ICD-10 system and were divided in non-affective (ICD-10 codes F20-F29) and affective psychoses (ICD-10 codes F30-F33). Blood tests carried out during the follow-up period were collated from clinical charts to evaluate the baseline fasting plasma glucose level upon starting APs treatment and at the time of follow-up (November 2016). The blood tests were done as part of clinical practice, to monitor metabolic changes during treatment. Fasting plasma glucose, triglycerides and cholesterol levels were determined by enzymatic procedures applying the Roche/Hitachi Modular D-P automated chemistry analyser and using the standard analytical system packs Glucose/God-pap, Cholesterol/CHOD cod-pap and Triglycerides/GPOpap. Abnormal glycaemia levels were defined based on the National Cholesterol Education Program (McIntyre et al. 2003) and World Health Organisation (Alberti and Zimmet 1998) criteria as follows: blood glucose ≥110 mg/dl for hyperglycemia and ≥126 mg/dl for diabetes. SPSS for Windows (version 23.0) was employed for statistical analyses.

The study design did not affect the clinical routine: the choice of antipsychotic and the dosage were entirely left to the treating psychiatrists. APs prescribed were divided into typical (e.g. Haloperidol, Fluphenazine, etc) and atypical (Risperidone, Aripiprazole, Olanzapine, Quetiapine and Clozapine). Chlorpromazine-equivalent doses were calculated based on standardized methods for comparing exposure to different APs drugs (Andreasen et al. 2010). The patients did not follow a standard exercise or diet regimen and were looked after by their clinicians as part of the usual care program. This study was performed with the approval of the Local Health Ethical Committee and informed consent was obtained from eligible patients.

2.3 Statistical analyses

We used parametric test procedures, the distribution of dependent variables being normal. The baseline mean fasting plasma glucose variance according to socio-demographic and clinical characteristics was investigated by an independent sample t-test. We used a dependent t-test to examine the time course of mean metabolic glycaemia values between baseline and follow-up. Finally, we performed linear multivariate regression analysis to adjust the association between migrant status and glycaemia level at follow up by gender, age, education, employment, APs treatment and dose.

3. Results

3.1 Sample description

Out of 105 patients who had contacts with CMHCs for FEP between 2010 and 2015, 50 agreed to take part in the study and 25 had blood test results available at follow-up (2016) and were therefore included. The follow-up period varied from patient to patient with a mean of 44.04 ± 17.75 months (range 16-82). All participants were treated with APs. Eleven patients also received antidepressants (AD) or mood stabilizers (MS). The sample's socio-demographic and clinical characteristics at baseline are described in Table 1. Fifty-two percent were men, had a mean age at onset of 28.56 years and were on average two years older at first contact with the CMHC, 32% were migrants (12% Asian, 12% African, 4% Hispanic and 4% European). Forty-eight percent were single and 52% had a high school diploma or higher qualification, 52% were employed and 48% were still living with the family of origin. Sixty-four percent had a DUP < 1 year. Sixty percent were diagnosed with non-affective psychosis (ICD-10 codes F20-F29), 40% with affective psychosis (ICD-10 codes F30-F33).

Three subjects started on haloperidol (mean dose: 4.33 ± 1.53 mg, chlorpromazine-equivalent dose: 276.84 ± 97.18 mg), 2 on fluphenazine (mean dose: 1.00 ± 0.00 mg, chlorpromazine-equivalent dose: 55.65 ± 0.00 mg), 5 on risperidone (mean dose: 3.40 ± 1.52 mg, chlorpromazine-equivalent dose: 42.65 ± 19.07 mg), 3 on aripiprazole (mean dose: 15.00 ± 5.00 mg, chlorpromazine- equivalent dose: 188.18 ± 62.73 mg), 6 on olanzapine (mean dose: 13.33 ± 7.53 mg, chlorpromazine- equivalent dose: 13.33 ± 141.29 mg) and 6 on quetiapine (mean dose: 425.00 ± 223.05 mg, chlorpromazine-equivalent dose: 242.17 ± 127.07 mg). Five started antidepressant or mood stabilizer co-therapy (three were treated with valproic acid and two were treated with paroxetine).

Cases	*n* %
Total	25 (100)
Male	13 (52)
Mean age (± SD)	30.56 ± 7.5
Mean age at onset (± SD)	28.56 ± 7.7
Marital status	
Single	12 (48)
Married	8 (32)
Divorced	3 (12)

Choabiting	2 (8)
Birth Origin	
Italy	17 (68)
Banglade	1 (4)
Brazil	1 (4)
India	1 (4)
Marocco	1 (4)
Iran	1 (4)
Tunisia	1 (4)
Moldavia	1 (4)
Camerun	1 (4)
Years of full time education	12 ± 3.8
Education	
Elementary school	1 (4)
Middle school	8 (32)
High school	5 (20)
Professional vocational school	5 (20)
University degree and above	6 (32)
Housing	
Private rental	3 (12)
Home owner	6 (24)
Living with a family	12 (48)
Other	4 (16)
Occupational Status	
Unemployed	12 (48)
Full time	9 (36)
Part time	3 (12)
Economically inactive	1 (4)
DUP	
<1 year	16 (64)
>= 1 Year	9 (36)
Diagnosis	
Non-affective psychoses	15 (60)
Affective psychoses	10 (40)
APs treatment	
Haloperidol	3 (12)
Fluphenazine	2 (8)
Risperidone	5 (20)
Aripiprazole	3 (12)
Olanzapine	6 (24)
Quetiapine	6 (24)
Co-therapy	
Citalopram	2 (8)

Carbolithium	1 (4)
Valproic acid	6 (24)
Paroxetine	2 (8)

FEP, First Episode Psychosis; BO, Bologna; SD, Standard deviation; DUP, Duration of Untreated Psychosis. See text for details

Table 1: FEP Bo West Sample socio-demographic and clinical characteristics.

3.2 Glycaemia course

At baseline the mean metabolic parameters were within the normal range. Two patients had hyperglycemia. We observed a significant increase in the mean fasting plasma glucose level (from 87.7 ± 16.1 to 97.3 ± 28.9, p=0.048). Two patients developed hyperglycemia and two diabetes (Table 2). The impact of socio-demographic and clinical characteristics on fasting plasma glucose is reported in Table 2. At baseline we observed a trend for mean fasting plasma glucose difference between men and women (81.92 ± 11.03 in males and 94.00 ± 18.68 in females; p=0.068 from independent sample t-test). Other groups (native vs migrant, white vs non-white, employed vs unemployed, compulsory education alone vs higher education, typical vs atypical APs therapy, no co-therapy vs co-therapy with AD and/or MS drugs) showed a slight non-significant mean variance.

We found that migrants showed a significantly higher increase in mean fasting plasma glucose. We observed a trend for significant increase in mean fasting plasma glucose among women. Moreover, we found that unemployed patients had a significantly higher increase in mean fasting plasma glucose levels. Finally, lower educated patients showed a significant increase in the mean fasting plasma glucose level. Other groups (ethnicity, APs treatment, AD and/or MS co-therapy) showed slight non-significant mean fasting plasma glucose changes during the follow-up period.

Characteristics	**Baseline Fasting Plasma Glucose**		**Last Fasting Plasma Glucose**		**% Patients Diagnosed[c]**	
	Mean ± Std.dev.	**P-value[a]**	**Mean ± Std.dev.**	**P-value[b]**	**Hypergly.**	**Diabetes**
Total	87.72 ± 16.08		97.32 ± 28.94	0.048**	24%	12%
Migration status						
Native	86.29 ± 12.35		87.53 ± 13.87	0.682	12%	0%
Migrant	90.75 ± 22.86	0.618	118.13 ± 41.28	0.040**	50%	38%
Ethnicity						
White	84.74 ± 12.56		89.37 ± 14.94	0.229	16%	0%
Non-white	97.17 ± 32.09	0.254	122.50 ± 47.06	0.134	50%	50%

Gender						
Male	81.92 ± 11.03		87.46 ± 15.20	0.336	8%	8%
Female	94.00 ± 18.68	0.068*	108.00 ± 36.55	0.090*****	42%	17%
Occupational status						
Employed	85.29 ± 11.78		88.07 ± 15.90	0.553	14%	7%
Unemployed	90.82 ± 20.53	0.438	109.09 ± 37.54	0.050******	36%	18%
Education						
Over CE	85.25 ± 11.69		87.81 ± 16.03	0.525	13%	6%
Compulsory edu.	92.11 ± 22.05	0.405	114.22 ± 39.092	0.052******	44%	22%
APs treatment						
Typical	86.20 ± 20.05		109.20 ± 46.61	0.222	40%	20%
Atypical	88.10 ± 15.54	0.851	94.35 ± 23.54	0.147	20%	10%
AD or MS co- therapy						
No	83.13 ± 11.76		98.00 ± 22.19	0.126	38%	13%
Yes	89.89 ± 17.67	0.271	97.00 ± 32.25	0.213	18%	12%

FEP, First Episode Psychosis; BO, Bologna; APs, antipsychotic medications; CE, compulsory education; AD, antidepressive medications; MS, mood stabilizer medications. [a]P-values are calculated from independent sample t-test; [b]P-values are calculated from dependent sample t-test; [c]% patients diagnosed hyperglycemia (fasting plasma glucose≥110mg/dL) and diabetes (fasting plasma glucose≥126mg/dL) on follow-up; **p≤0.05; *p≤0.1

Table 2: FEP Bo West sample fasting plasma glucose changes according to the socio-demographic and clinical characteristics.

Multiple linear regression analysis including gender, age, occupation status, level of education, and history of migration revealed that only migrant status was a significant determinant of fasting plasma glucose level at follow up (β=0.404; p=0.028). When including in the model the kind of AP treatment (typical vs atypical) and the chlorpromazine-equivalent APs dosage, the association between migrant status and mean fasting plasma glucose level at follow-up still showed a trend for statistical significance (β=0.312; p=0.111). No other factors added in the linear regression model showed any significant association with the mean fasting plasma glucose level at follow-up.

4. Discussion

We found a significant mean fasting plasma glucose increase during APs treatment; this result is consistent with those of previous studies (Tsygankov et al. 2014; Whicher et al. 2018). Our study adds to the already available evidence that the strongest factor predicting an elevated mean fasting plasma glucose level at follow-up is the patient's history of migration. The present study on APs-related hyperglycemia and other metabolic disorders is one of the few follow-up research projects carried out among an incidence cohort of FEP patients in an everyday clinical

setting designed independently of drug companies. These results are, in our opinion, valuable because the patients enrolled were completely drug naïve and representative of the FEP population in our catchment area.

This study to our knowledge is the first one to suggest that FEP migrants are at greater risk of developing metabolic disorders such as hyperglycemia and type II diabetes during APs treatment. Previous studies focusing on ethnicity found that African-American and Hispanic ethnicity are associated with an increased prevalence of diabetes, while European ethnicity is associated with a decreased risk of developing diabetes during APs treatment (Ward and Druss 2015). Thus, patients with a history of migration should be even more carefully monitored than other drug- naïve patients from the very first few weeks of treatment, to limit these adverse effects.

The limitations of our study are the naturalistic study design (lack of standardized diet and treatment programmes). Moreover, the small sample size limited statistical power, which was sufficient only to observe large effect sizes. Clearly, further research with larger samples and a control group is needed to characterize the specific role of different APs in the development of metabolic side effects.

Acknowledgements

We acknowledge the contribution of the entire Bologna - FEP Study team. We wish to thank the patients and clinical staff of the Bologna-CMHCs.

Conflicts of Interest

The authors declare that they have no competing interests.

References

1. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO Consultation. Diabet Med 15 (1998): 539-553.
2. Andreasen NC, Pressler M, Nopoulos P, et al. Antipsychotic Dose Equivalents and Dose-Years: A Standardized Method for Comparing Exposure to Different Drugs. Biol. Psychiatry 67 (2010): 255-262.
3. Correll CU, Detraux J, De Lepeleire J, et al. Effects of antipsychotics, antidepressants and mood stabilizers on risk for physical diseases in people with schizophrenia, depression and bipolar disorder. World Psychiatry 14 (2015): 119-136.
4. Dixon L, Weiden P, Delahanty J, et al. Prevalence and correlates of diabetes in national schizophrenia samples. Schizophr. Bull 26 (2000): 903-912.
5. Hare-Bruun H, Flint A, Heitmann BL. Glycemic index and glycemic load in relation to changes in body weight, body fat distribution, and body composition in adult Danes. Am. J. Clin. Nutr 84 (2006): 871-879.
6. Heraclides AM, Chandola T, Witte DR, et al. Work Stress, Obesity and the Risk of Type 2 Diabetes: Gender-Specific Bidirectional Effect in the Whitehall II Study. Obesity 20 (2012): 428-433.

7. Katchunga P, Masumbuko B, Belma M, et al. Age and living in an urban environment are major determinants of diabetes among South Kivu Congolese adults. Diabetes Metab 38 (2012): 324-331.
8. Krajnak KM. Potential Contribution of Work-Related Psychosocial Stress to the Development of Cardiovascular Disease and Type II Diabetes: A Brief Review. Environ. Health Insights 8 (2014): 41-45
9. Lanting LC, Joung IMA, Mackenbach JP, et al. Ethnic differences in mortality, end-stage complications, and quality of care among diabetic patients: a review. Diabetes Care 28 (2005): 2280-2288.
10. Mamakou V, Hackinger S, Zengini E, et al. Combination therapy as a potential risk factor for the development of type 2 diabetes in patients with schizophrenia: the GOMAP study. BMC Psychiatry (2018): 249.
11. Mamakou V, Thanopoulou A, Gonidakis F, et al. Schizophrenia and type 2 diabetes mellitus. Psychiatriki 29 (2018): 64-73.

Citation: Gianmarco Iuzzolino, Giuseppe D'Andrea, Tiziano De Matteis, Lorenzo Guidi, Domenico Berardi, Ilaria Tarricone. Hyperglycemia and FEP: Does Migration Status Matter?. Journal of Psychiatry and Psychiatric Disorders 4 (2020): 1-9.