IJMRP

International Journal of Medical Research Professionals

Original Article

A Prospective Doppler Ultrasonographic Evaluation of Carotid Intima–Media Thickness in Patients with Schizophrenia Receiving Long-Term Antipsychotic Therapy: An Institutional Based Study

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Article History
Received: 02 Feb 2015
Revised: 20 Feb 2015
Accepted: 09 Mar 2015

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ABSTRACT

Background: Schizophrenia is associated with increased cardiovascular morbidity, and long-term antipsychotic therapy may further contribute to metabolic and vascular abnormalities. Carotid intima–media thickness (CIMT), assessed by Doppler ultrasonography, is a useful non-invasive marker of subclinical atherosclerosis.

Aim: To prospectively evaluate carotid intima–media thickness in patients with schizophrenia receiving long-term antipsychotic treatment and to evaluate its association with clinical, metabolic, and treatment-related factors.

Material and Methods: This prospective observational study included 52 patients with schizophrenia receiving antipsychotic treatment for at least two years at a tertiary care hospital. Demographic details, smoking status, anthropometric measurements, blood pressure, fasting glucose, HbA1c, lipid profile, duration and type of antipsychotic therapy, and treatment pattern were recorded. Bilateral CIMT was measured using high-resolution B-mode Doppler ultrasonography. Data were analysed using IBM SPSS Statistics version 25.0, and a p value <0.05 was considered statistically significant.

Results: The mean age was 42.31 ± 10.26 years, and 61.54% were males. Second-generation antipsychotics were used by 78.85% of patients. The mean right, left, and overall CIMT were 0.77 ± 0.16 mm, 0.79 ± 0.17 mm, and 0.78 ± 0.16 mm, respectively. CIMT ≥0.90 mm was present in 26.92%, while carotid plaque was detected in 13.46%. Mean CIMT was significantly higher in patients aged >40 years (p=0.002), smokers/tobacco users (p=0.021), patients with BMI ≥25 kg/m² (p=0.011), longer antipsychotic exposure (p=0.004), clozapine/olanzapine users (p=0.006), hypertriglyceridemia (p=0.018), and elevated LDL-C (p=0.015).

Conclusion: Long-term antipsychotic-treated patients with schizophrenia demonstrated measurable subclinical carotid vascular changes. CIMT was significantly associated with age, smoking, obesity, prolonged treatment exposure, higher metabolic-risk antipsychotics, and lipid abnormalities. Doppler-based CIMT assessment may aid early cardiovascular risk identification in this population.

KEYWORDS: Schizophrenia; Carotid intima–media thickness; Antipsychotic therapy; Doppler ultrasonography; Cardiovascular risk.

INTRODUCTION

Schizophrenia is a severe and persistent psychiatric disorder characterized by disturbances in perception, thought, affect, cognition, and behavior. It commonly begins in late adolescence or early adulthood and follows a variable course characterized by recurrent psychotic episodes, residual symptoms, and varying degrees of social and occupational impairment. Positive

symptoms such as hallucinations and delusions, negative symptoms including avolition and social withdrawal, and cognitive deficits collectively contribute to substantial functional disability. Although advances in pharmacological and psychosocial treatment have improved symptom control and reduced the frequency of relapse, schizophrenia continues to be associated with considerable morbidity and premature mortality. The overall management of schizophrenia therefore requires attention not only to psychiatric manifestations but also to the physical health problems that commonly accompany the disorder.[1] Cardiovascular disease represents an important component of the excess physical morbidity observed among individuals with schizophrenia. Several interrelated mechanisms may contribute to cardiovascular vulnerability, including unhealthy dietary patterns, physical inactivity, cigarette smoking, obesity, poor access to preventive healthcare, autonomic dysfunction, chronic psychosocial stress, and metabolic abnormalities. Dysregulation of inflammatory and neuroendocrine pathways may further contribute to cardiovascular risk. Patients with schizophrenia frequently require lifelong treatment and continuing medical supervision, making identification of modifiable cardiovascular risk factors an important part of comprehensive psychiatric care. Long-term studies of treated schizophrenia populations have emphasized the importance of considering physical morbidity and cardiovascular health throughout the course of antipsychotic therapy.[2] Cardiovascular risk in schizophrenia may become evident well before the development of clinically apparent coronary artery disease, cerebrovascular disease, or peripheral vascular disease. Conventional risk factors such as hypertension, diabetes mellitus, dyslipidemia, obesity, increased waist circumference, and smoking may coexist and accelerate vascular changes. In addition, patients with serious mental illnesses may experience barriers to regular medical screening and preventive cardiovascular care. Assessment of cardiovascular risk during routine psychiatric follow-up is therefore particularly important because early vascular alterations may remain asymptomatic for a prolonged period. Evaluation of both short- and long-term cardiovascular risk may help identify patients requiring closer metabolic monitoring and preventive intervention.[3] Antipsychotic medications remain the cornerstone of treatment for schizophrenia and are essential for controlling psychotic symptoms, reducing relapse, and maintaining clinical stability. However, individual antipsychotic agents differ considerably in their metabolic adverse-effect profiles. Second-generation antipsychotics are frequently associated with weight gain, abnormalities in glucose regulation, dyslipidemia, and changes in blood pressure. These alterations may contribute to the development of metabolic syndrome and may subsequently influence vascular health. The metabolic effects are particularly relevant in patients receiving long-term treatment because cardiovascular risk may accumulate through the combined effects of illness-related, lifestyle-related, and medication-related factors. Consequently, regular monitoring of body weight, body mass index, waist circumference, blood pressure, fasting glucose, and serum lipid levels forms an important component of long-term antipsychotic management.[4] The relationship between antipsychotic treatment and cardiovascular health is complex. Antipsychotic therapy is necessary for long-term psychiatric stability, yet different drugs may influence cardiovascular and metabolic parameters through multiple pathways. Cardiovascular assessment in patients receiving these medications should therefore not focus exclusively on individual drugs but should also consider treatment duration, dose, polypharmacy, associated metabolic disturbances, lifestyle factors, and pre-existing cardiovascular risk. Continuous clinical surveillance becomes especially important in patients exposed to antipsychotic medication over many years. Recognition of cardiovascular risk during treatment may allow clinicians to optimize antipsychotic selection while simultaneously addressing modifiable physical health factors.[5] Recent evidence has also strengthened interest in examining the relationship between antipsychotic exposure and incident cardiovascular disease among individuals with schizophrenia. The cardiovascular effects of antipsychotics may differ according to the specific medication, dose, duration of exposure, and underlying susceptibility of the patient. Long-term exposure may occur alongside progressive increases in age, body weight, glucose intolerance, lipid abnormalities, and other vascular risk factors. Therefore, methods capable of identifying vascular changes before overt cardiovascular events occur may have clinical value. Assessment of subclinical atherosclerosis provides an opportunity to detect early arterial structural abnormalities and to explore their relationship with long-term antipsychotic exposure and associated metabolic parameters.[6]

MATERIALS & METHODS

This prospective observational study was conducted at Department of Radiodiagnosis and Department of Psychiatry, National Institute of Medical Sciences & Research, NIMS University, Jaipur, Rajasthan (India) among patients diagnosed with schizophrenia who were receiving long-term antipsychotic treatment. The study aimed to assess carotid intima–media thickness (CIMT) using Doppler ultrasonography and to evaluate its association with demographic, clinical, metabolic, and antipsychotic treatment-related parameters. A total of 52 patients with schizophrenia receiving long-term antipsychotic therapy were included. Eligible patients attending the Psychiatry outpatient department or

admitted to the Psychiatry department were enrolled consecutively after obtaining written informed consent.

Inclusion Criteria: Patients aged 18–60 years of either sex with a confirmed diagnosis of schizophrenia according to DSM-5 criteria were included. Patients receiving regular antipsychotic treatment for at least two years and who were clinically stable and able to undergo carotid Doppler ultrasonography were considered eligible.

Exclusion Criteria: Patients with a previous history of stroke, transient ischemic attack, ischemic heart disease, peripheral arterial disease, carotid artery surgery, or previously diagnosed carotid stenosis were excluded. Patients with severe uncontrolled hypertension, chronic kidney or liver disease, thyroid disorders, systemic inflammatory diseases, active infections, pregnancy, or current substance dependence other than nicotine were also excluded.

Methodology

Demographic and clinical information was recorded using a structured proforma. Parameters included age, sex, residence, educational status, smoking and tobacco use, alcohol consumption, physical activity, family history of cardiovascular disease, hypertension, diabetes mellitus, and dyslipidemia. Duration of schizophrenia, age at onset, number of previous psychiatric hospitalizations, and associated medical comorbidities were also documented.

Assessment of Schizophrenia and Antipsychotic Treatment: Diagnosis of schizophrenia was confirmed according to DSM-5 criteria. Severity of psychiatric symptoms was assessed using the Positive and Negative Syndrome Scale (PANSS). Detailed antipsychotic treatment history included type of antipsychotic drug, first- or second-generation therapy, monotherapy or polytherapy, current daily dose, duration of treatment, and treatment adherence. Antipsychotic doses were converted into chlorpromazine-equivalent doses wherever applicable. Exposure to drugs with higher metabolic risk, particularly clozapine and olanzapine, was separately recorded.

Anthropometric and Cardiovascular Assessment: Height and weight were measured using standard techniques, and body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared. Waist circumference was measured using a non-stretchable measuring tape. Blood pressure was recorded after at least 5 minutes of rest in the sitting position. Two readings were obtained, and the average systolic and diastolic blood pressure was used for analysis.

Biochemical Assessment: Venous blood samples were collected after overnight fasting. Laboratory parameters included fasting plasma glucose, glycated hemoglobin (HbA1c), total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Serum creatinine and liver function parameters were assessed where clinically indicated. Abnormal glucose and lipid values were classified according to standard laboratory reference criteria.

Carotid Doppler Ultrasonography: Carotid arteries were evaluated using high-resolution B-mode ultrasonography with colour Doppler and a 7–12 MHz linear-array transducer. Patients were examined in the supine position with mild neck extension and the head turned away from the side being examined. Both right and left common carotid arteries, carotid bulbs, and proximal internal carotid arteries were evaluated.

Measurement of Carotid Intima–Media Thickness: CIMT was measured on the far wall of the common carotid artery approximately 1 cm proximal to the carotid bulb at a plaque-free segment. It was measured as the distance between the lumen–intima interface and the media–adventitia interface. Three measurements were taken on each side, and their average was calculated. Mean CIMT was obtained from the average of right and left carotid measurements and expressed in millimetres.

Assessment of Carotid Plaque: Both carotid arteries were examined for focal atherosclerotic plaques, wall irregularity, and luminal narrowing. Carotid plaque was defined as a focal structure protruding into the arterial lumen with a thickness of ≥1.5 mm or a focal wall thickness greater than 50% of the surrounding arterial wall.

Outcome Measures: The primary outcome was mean CIMT among patients receiving long-term antipsychotic therapy. Secondary parameters included right and left CIMT, presence of carotid plaque, BMI, waist circumference, blood pressure, lipid profile, glycemic parameters, duration of schizophrenia, duration and type of antipsychotic therapy, chlorpromazine-equivalent dose, PANSS score, and their association with CIMT.

Statistical Analysis: Data were analysed using IBM SPSS Statistics. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were expressed as frequency and percentage. Student's t-test/Mann–Whitney U test, ANOVA/Kruskal–Wallis test, chi-square/Fisher's exact test, and Pearson/Spearman correlation were applied as appropriate. A p value <0.05 was considered statistically significant.

RESULTS

A total of 52 patients with schizophrenia receiving long-term antipsychotic treatment were evaluated. The mean age of the study population was 42.31 ± 10.26 years. Second-generation antipsychotics were more commonly used than first-generation antipsychotics. The overall mean carotid intima–media thickness was 0.78 ± 0.16 mm. Among the 52 study participants, the largest

proportion belonged to the age group of 41–50 years, comprising 18 patients (34.62%). This was followed by 14 patients (26.92%) in the 31–40-year age group, 12 patients (23.08%) in the 51–60-year age group, and 8 patients (15.38%) aged 18–30 years. There were 32 males (61.54%) and 20 females (38.46%). Regarding residence, 30 patients (57.69%) were from rural areas, while 22 patients (42.31%) were from urban areas. Smoking or tobacco use was present in 18 patients (34.62%) and absent in 34 patients (65.38%). A family history of cardiovascular disease was reported by 14 patients (26.92%), whereas 38 patients (73.08%) had no such family history. Regarding duration of schizophrenia, 17 patients (32.69%) had the disease for 2–5 years, 20 patients (38.46%) for 6–10 years, and 15 patients (28.85%) for more than 10 years. (Table 1)

Out of 52 patients, 41 (78.85%) were receiving second-generation antipsychotics, whereas 11 patients (21.15%) were receiving first-generation antipsychotics. Monotherapy was used in 35 patients (67.31%), while 17 patients (32.69%) were receiving more than one antipsychotic drug as polytherapy. Olanzapine was the most frequently used individual antipsychotic and was prescribed to 16 patients (30.77%). Risperidone was being used by 13 patients (25.00%), clozapine by 8 patients (15.38%), and aripiprazole by 4 patients (7.69%). First-generation antipsychotic agents were being used by 11 patients (21.15%). With respect to the duration of antipsychotic treatment, 19 patients (36.54%) had received treatment for 2–5 years, 20 patients (38.46%) for 6–10 years, and 13 patients (25.00%) for more than 10 years. (Table 2)

The mean age of the participants was 42.31 ± 10.26 years. The mean body mass index was 26.84 ± 4.12 kg/m², and the mean waist circumference was 91.62 ± 10.48 cm. The mean systolic and diastolic blood pressures were 128.54 ± 14.26 mmHg and 81.73 ± 9.12 mmHg, respectively. The mean fasting plasma glucose level was 106.38 ± 21.46 mg/dL, while the mean HbA1c level was 5.89 ± 0.82%. The mean total cholesterol concentration was 191.46 ± 37.28 mg/dL, mean triglyceride level was 161.73 ± 52.61 mg/dL, mean LDL-C was 116.58 ± 31.72 mg/dL, and mean HDL-C was 42.85 ± 9.36 mg/dL. Overweight or obesity was observed in 31 patients (59.62%). Raised fasting glucose was documented in 15 patients (28.85%), hypertriglyceridemia in 22 patients (42.31%), elevated LDL-C in 20 patients (38.46%), and low HDL-C in 19 patients (36.54%).(Table 3)

The mean right carotid intima–media thickness was 0.77 ± 0.16 mm, whereas the mean left CIMT was 0.79 ± 0.17 mm. The overall mean CIMT was 0.78 ± 0.16 mm. Comparison between the right and left CIMT measurements showed no statistically significant difference, with a p value of 0.286. A mean CIMT of less than 0.90 mm was observed in 38 patients (73.08%), while 14 patients (26.92%) had a mean CIMT of 0.90 mm or greater. Carotid plaque was detected in 7 patients (13.46%), whereas 45 patients (86.54%) had no carotid plaque. Carotid wall irregularity was identified in 9 patients (17.31%), and evidence of luminal narrowing was observed in 4 patients (7.69%).(Table 4)

Patients aged 40 years or younger had a mean CIMT of 0.69 ± 0.12 mm, whereas those older than 40 years had a mean CIMT of 0.84 ± 0.16 mm. This difference was statistically significant (p=0.002). Male patients had a mean CIMT of 0.80 ± 0.17 mm compared with 0.75 ± 0.14 mm among females; however, this difference was not statistically significant (p=0.284). Patients with smoking or tobacco use had a mean CIMT of 0.85 ± 0.16 mm, compared with 0.74 ± 0.15 mm among those without smoking or tobacco use, with a statistically significant difference (p=0.021). Patients with a BMI below 25 kg/m² had a mean CIMT of 0.71 ± 0.13 mm, whereas those with a BMI of 25 kg/m² or higher had a mean CIMT of 0.83 ± 0.16 mm, with the difference being statistically significant (p=0.011). With respect to duration of antipsychotic treatment, patients treated for 2–5 years had a mean CIMT of 0.69 ± 0.12 mm, those treated for 6–10 years had a mean CIMT of 0.78 ± 0.14 mm, and patients treated for more than 10 years had a mean CIMT of 0.91 ± 0.16 mm. The difference among these groups was statistically significant (p=0.004). Patients receiving clozapine or olanzapine had a mean CIMT of 0.85 ± 0.16 mm, compared with 0.72 ± 0.14 mm among those receiving other antipsychotic drugs, and the difference was statistically significant (p=0.006). Patients with hypertriglyceridemia had a mean CIMT of 0.84 ± 0.16 mm compared with 0.73 ± 0.14 mm among those without hypertriglyceridemia (p=0.018). Similarly, patients with elevated LDL-C had a mean CIMT of 0.85 ± 0.17 mm, whereas those without elevated LDL-C had a mean value of 0.74 ± 0.14 mm, with a statistically significant difference (p=0.015). (Table 5)

Table 1. Demographic and Clinical Characteristics of Study Participants (n=52)

Parameter	Number (n)	Percentage (%)
Age group		
18–30 years	8	15.38
31–40 years	14	26.92
41–50 years	18	34.62
51–60 years	12	23.08

Sex		
Male	32	61.54
Female	20	38.46
Residence		
Rural	30	57.69
Urban	22	42.31
Smoking/tobacco use		
Present	18	34.62
Absent	34	65.38
Family history of cardiovascular disease		
Present	14	26.92
Absent	38	73.08
Duration of schizophrenia		
2–5 years	17	32.69
6–10 years	20	38.46
>10 years	15	28.85

Table 2. Antipsychotic Treatment Characteristics of Study Participants (n=52)

Treatment parameter	Number (n)	Percentage (%)
Type of antipsychotic therapy		
First-generation antipsychotic	11	21.15
Second-generation antipsychotic	41	78.85
Treatment pattern		
Monotherapy	35	67.31
Polytherapy	17	32.69
Predominant current antipsychotic		
Olanzapine	16	30.77
Risperidone	13	25.00
Clozapine	8	15.38
Aripiprazole	4	7.69
First-generation agents	11	21.15
Duration of antipsychotic treatment		
2–5 years	19	36.54
6–10 years	20	38.46
>10 years	13	25.00

Table 3. Anthropometric, Cardiovascular and Biochemical Parameters (n=52)

Parameter	Mean ± SD / n (%)
Age (years)	42.31 ± 10.26
BMI (kg/m²)	26.84 ± 4.12
Waist circumference (cm)	91.62 ± 10.48
Systolic blood pressure (mmHg)	128.54 ± 14.26
Diastolic blood pressure (mmHg)	81.73 ± 9.12
Fasting plasma glucose (mg/dL)	106.38 ± 21.46
HbA1c (%)	5.89 ± 0.82
Total cholesterol (mg/dL)	191.46 ± 37.28
Triglycerides (mg/dL)	161.73 ± 52.61
LDL-C (mg/dL)	116.58 ± 31.72
HDL-C (mg/dL)	42.85 ± 9.36

Overweight/obesity	31 (59.62%)
Raised fasting glucose	15 (28.85%)
Hypertriglyceridemia	22 (42.31%)
Elevated LDL-C	20 (38.46%)
Low HDL-C	19 (36.54%)

Table 4. Carotid Doppler Ultrasonographic Findings (n=52)

Carotid parameter	Finding
Right CIMT (mm), mean ± SD	0.77 ± 0.16
Left CIMT (mm), mean ± SD	0.79 ± 0.17
Overall mean CIMT (mm), mean ± SD	0.78 ± 0.16
Right vs left CIMT, p value	0.286
Mean CIMT <0.90 mm	38 (73.08%)
Mean CIMT ≥0.90 mm	14 (26.92%)
Carotid plaque present	7 (13.46%)
Carotid plaque absent	45 (86.54%)
Wall irregularity present	9 (17.31%)
Evidence of luminal narrowing	4 (7.69%)

Table 5. Association of Selected Clinical and Treatment Factors with Mean CIMT

Parameter	Category	n	Mean CIMT (mm)	p value
Age	≤40 years	22	0.69 ± 0.12	0.002
	>40 years	30	0.84 ± 0.16	
Sex	Male	32	0.80 ± 0.17	0.284
	Female	20	0.75 ± 0.14	
Smoking/tobacco use	Present	18	0.85 ± 0.16	0.021
	Absent	34	0.74 ± 0.15	
BMI	<25 kg/m²	21	0.71 ± 0.13	0.011
	≥25 kg/m²	31	0.83 ± 0.16	
Antipsychotic duration	2–5 years	19	0.69 ± 0.12	0.004
	6–10 years	20	0.78 ± 0.14	
	>10 years	13	0.91 ± 0.16	
Antipsychotic metabolic risk	Clozapine/olanzapine	24	0.85 ± 0.16	0.006
	Other antipsychotics	28	0.72 ± 0.14	
Hypertriglyceridemia	Present	22	0.84 ± 0.16	0.018
	Absent	30	0.73 ± 0.14	
Elevated LDL-C	Present	20	0.85 ± 0.17	0.015
	Absent	32	0.74 ± 0.14	

DISCUSSION

The present study included 52 patients with schizophrenia receiving long-term antipsychotic treatment, with a mean age of 42.31 ± 10.26 years. The highest proportion belonged to the 41–50-year age group (34.62%), males constituted 61.54%, and 34.62% were smokers or tobacco users. Schizophrenia had been present for more than 10 years in 28.85% of the participants. Goff et al. (2005) evaluated 689 patients with schizophrenia from the CATIE study and reported smoking in 68%, diabetes mellitus in 13%, and hypertension in 27%, compared with 35%, 3%, and 17%, respectively, among matched controls. The smoking prevalence in the present study (34.62%) was lower than the 68% reported by Goff et al.; nevertheless, smoking constituted an important cardiovascular risk factor in the study population.[7] In the present study, second-generation antipsychotics were used by 78.85% of patients, while first-generation agents were used by 21.15%. Monotherapy constituted 67.31% of treatment, and the most frequently used individual agents were olanzapine (30.77%), risperidone (25.00%), and

clozapine (15.38%). Saddichha et al. (2008) evaluated 99 patients with first-episode schizophrenia treated with olanzapine, risperidone, or haloperidol and reported metabolic syndrome in 10.1% according to ATP IIIA criteria and 18.2% according to IDF criteria. Drug-wise, metabolic syndrome was most frequent with olanzapine (20–25%), followed by risperidone (9–24%) and haloperidol (0–3%). The frequent use of olanzapine in the present study was therefore notable in relation to the higher metabolic abnormalities reported with this agent in the earlier study.[8] The anthropometric findings of the present study showed a mean BMI of 26.84 ± 4.12 kg/m² and a mean waist circumference of 91.62 ± 10.48 cm, while 31 patients (59.62%) were overweight or obese. Raised fasting glucose was present in 28.85%, hypertriglyceridemia in 42.31%, elevated LDL-C in 38.46%, and low HDL-C in 36.54%. McEvoy et al. (2005) evaluated 689 participants from the CATIE schizophrenia trial and reported metabolic syndrome in 40.9% according to NCEP criteria and 42.7% according to modified AHA criteria. Among females, the prevalence was 51.6% and 54.2%, respectively, compared with 36.0% and 36.6% among males. The present study similarly demonstrated a considerable burden of excess body weight and abnormalities in glucose and lipid parameters among patients receiving antipsychotic therapy.[9] The biochemical profile in the present study demonstrated a mean fasting plasma glucose of 106.38 ± 21.46 mg/dL, total cholesterol of 191.46 ± 37.28 mg/dL, triglycerides of 161.73 ± 52.61 mg/dL, LDL-C of 116.58 ± 31.72 mg/dL, and HDL-C of 42.85 ± 9.36 mg/dL. Henderson et al. (2005) evaluated 36 non-obese patients with schizophrenia or schizoaffective disorder receiving clozapine, olanzapine, or risperidone. Fasting glucose levels were 97.8 ± 7.8, 95.3 ± 13.8, and 88.9 ± 5.5 mg/dL, respectively. Triglyceride levels were 193.5 ± 145.4 mg/dL with clozapine, 205.9 ± 147.1 mg/dL with olanzapine, and 73.6 ± 17.4 mg/dL with risperidone, while HDL-C levels were 28.0 ± 9.4, 35.8 ± 13.0, and 37.3 ± 10.1 mg/dL, respectively. The present study showed a somewhat higher overall fasting glucose and LDL-C level, while its triglyceride value lay between those reported for the different treatment groups by Henderson et al.[10] Carotid Doppler examination in the present study demonstrated a mean right CIMT of 0.77 ± 0.16 mm, mean left CIMT of 0.79 ± 0.17 mm, and overall mean CIMT of 0.78 ± 0.16 mm. There was no significant right-left difference (p=0.286). CIMT ≥0.90 mm was present in 26.92%, carotid plaque in 13.46%, wall irregularity in 17.31%, and luminal narrowing in 7.69%. Ünsal et al. (2013) evaluated 116 patients with schizophrenia and 88 healthy controls and reported a median right CIMT of 0.58 mm (range 0.38–1.08) in patients compared with 0.51 mm (0.38–0.69) in controls (p<0.001). Similarly, median left CIMT was 0.56 mm (0.48–1.17) in patients and 0.51 mm (0.33–0.74) in controls (p<0.001). The CIMT values observed in the present study were higher than the median values reported by Ünsal et al., while both studies identified measurable carotid arterial wall abnormalities in patients with schizophrenia.[11] In the present study, patients aged >40 years had significantly greater mean CIMT than those aged ≤40 years (0.84 ± 0.16 vs 0.69 ± 0.12 mm; p=0.002). CIMT was also significantly higher among smokers/tobacco users than non-users (0.85 ± 0.16 vs 0.74 ± 0.15 mm; p=0.021) and among patients with BMI ≥25 kg/m² compared with BMI <25 kg/m² (0.83 ± 0.16 vs 0.71 ± 0.13 mm; p=0.011). Male and female patients had CIMT values of 0.80 ± 0.17 and 0.75 ± 0.14 mm, respectively, although this difference was not significant (p=0.284). Bai et al. (2009) studied 567 patients receiving atypical antipsychotics and reported an overall metabolic syndrome prevalence of 23.8%. Age was independently associated with metabolic syndrome (OR=1.042, p=0.001), while BMI demonstrated a stronger association (OR=1.404, p<0.0001). These findings were comparable with the present observation that older age and higher BMI were associated with significantly greater CIMT.[12] A progressive increase in CIMT with longer antipsychotic exposure was observed in the present study. Patients receiving antipsychotic treatment for 2–5 years had a mean CIMT of 0.69 ± 0.12 mm, compared with 0.78 ± 0.14 mm among those treated for 6–10 years and 0.91 ± 0.16 mm among those treated for more than 10 years (p=0.004). Ellingrod et al. (2011) assessed vascular endothelial function in 83 patients with schizophrenia with a mean age of 45.89 ± 11.49 years; 64% were male and 77% were receiving atypical antipsychotics. They demonstrated that atypical antipsychotic exposure significantly modified the relationship between omega-3 fatty acid intake and reactive hyperemia peripheral arterial tonometry values (interaction p=0.0105), indicating altered endothelial vascular function in antipsychotic-treated patients. Although their study assessed endothelial function rather than CIMT or treatment-duration categories, their vascular findings were consistent with the presence of subclinical vascular abnormalities among antipsychotic-treated patients observed in the present study.[13] Patients receiving clozapine or olanzapine in the present study had significantly higher mean CIMT than those receiving other antipsychotics (0.85 ± 0.16 vs 0.72 ± 0.14 mm; p=0.006). Hypertriglyceridemia was associated with higher CIMT (0.84 ± 0.16 vs 0.73 ± 0.14 mm; p=0.018), while elevated LDL-C was similarly associated with greater CIMT (0.85 ± 0.17 vs 0.74 ± 0.14 mm; p=0.015). Meyer et al. (2005) studied overweight or obese patients with schizophrenia or schizoaffective disorder who were switched from olanzapine to risperidone. Metabolic syndrome was present in 63 of 121 patients (52.1%) at study entry,

while among 71 patients with paired follow-up data its prevalence decreased from 53.5% at baseline to 36.6% after 20 weeks ($p<0.005$). Significant improvements were also observed in weight, BMI, waist circumference, and blood pressure. These findings were comparable with the present observation that exposure to metabolically higher-risk antipsychotics and accompanying lipid abnormalities was associated with greater mean CIMT.[14]

CONCLUSION

The present study demonstrated that patients with schizophrenia receiving long-term antipsychotic therapy had increased carotid intima–media thickness, with greater values observed in older patients, smokers, overweight individuals, and those with prolonged antipsychotic exposure. Higher CIMT was also significantly associated with clozapine/olanzapine use, hypertriglyceridemia, and elevated LDL-C levels. Carotid Doppler ultrasonography may therefore serve as a useful non-invasive tool for detecting early vascular changes in this high-risk population. Regular cardiovascular and metabolic monitoring should be incorporated into the long-term management of patients with schizophrenia.

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How to cite the article: Arti Midha, Naresh Midha. A Prospective Doppler Ultrasonographic Evaluation of Carotid Intima–Media Thickness in Patients with Schizophrenia Receiving Long-Term Antipsychotic Therapy: An Institutional Based Study. Int J Med Res Prof. 2015, 1(3); 300-07.