

Case Report

Incidence of Weight Gain and Hyper Lipidemia with a Typical Antipsychotic Treatment: A Prospective Community Based Clinical Study

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Abstract

Atypical Antipsychotic (AAPS) have been found to be effective in various psychiatric conditions however evidence of treatment, emergent weight gain and hyperlipidemia limit their clinical benefits.

Objective: To determine the incidence of treatment emergent weight gain and hyperlipidemia with atypical antipsychotics.

Method: Patients with schizophrenic and non-schizophrenic conditions were randomly started on AAPS. Weight, BMI, triglycerides were measured every 3 months from the base line for one year.

121 enrolled, 119 completed the one year follow up study.

Male : 69; Female: 50; Olanzapine: 51; Risperidone: 59; Quetiapine: 8; Clozapine: 1.

Data Analysis: Descriptive and inferential analysis was carried out except Clozapine to examine the effects on weight, BMI and triglycerides.

Limitations: Polypharmacy and ethnicity were not considered.

Results:

Mean Weight Gain:

Males: Risperidone 7.5 kg > Olanzapine 5.353 kg > Quetiapine 4.43 KG.
Females: Olanzapine 4.71 grams > Quetiapine 3.81 grams > Risperidone 3.14 kg.

Percentage of weight gain – more than 7%:

Males: Risperidone 46% > Quetiapine 33% > Olanzapine 16%
Females: Quetiapine 40% > Olanzapine 35% > Risperidone 9%

BMI

Overweight:

Males: Quetiapine 100% > Olanzapine 58.06% > Risperidone 51.35%
Females: Quetiapine 80% > Risperidone 50% > Olanzapine 45%

Obesity

Males: Quetiapine 33.33% > Olanzapine 32.26% > Risperidone 16.22%
Females: Risperidone 50% > Quetiapine 20% > Olanzapine 20%

Mean Triglycerides

Males: Risperidone 1.92 > Olanzapine 1.7
Females: Olanzapine 1.97 > Risperidone 1.78

Percentage of Hyperlipidemia

Males: Olanzapine 54.84% > Risperidone 43.24% > Quetiapine 33.33%
Females: Quetiapine 80% > Olanzapine 65% > Risperidone 45.45%

Hyper Lipidemia Related to Age and Disease

Risperidone - Mostly seen in the 20 to 40 years age group

Olanzapine - Mostly seen in 61 years plus.

Olanzapine seems to be having more propensity to induce hyper-lipidemia in Schizophrenia and Bi-polar disorder.

Odd ratio

Olanzapine Vs Risperidone - 1.81% (S.e.(O) 0.70034827).

Conclusion: The results show that atypical antipsychotic do affect weight, BMI and Triglycerides in varying degree and in relation to age, gender and disease which has significant clinical implications that warrant close monitoring with ongoing education on life style, diet and exercise in a heuristic manner.

Introduction & Background

Patients with chronic psychiatric disorders are at increased risk for morbidity and mortality resulting from various medical diseases including respiratory diseases, infectious diseases, obesity, diabetes mellitus and cardiovascular disease [1].

In patients with schizophrenia and affective disorder the prevalence of risk factor for cardiovascular disease is approximately 1.5 to 2 times higher than the rate in the general population [2].

Mood disorders associated with obesity and it has been postulated gluco-corticoids play a central role in that role in the patho genesis of metabolic syndrome [3,4].

It has been evidenced all atypical antipsychotics induce weight gain and hyperlipidemia [5-7]. However, nearly all psychotropic medications induce weight gain [8-10].

The use of the atypical anti-psychotics is not confined to the treatment of schizophrenia but used to treat a broad array of other psychiatric disorders for which it has been found effective [11].

Recently there is a general consensus of varying adverse effects on weight and triglycerides with atypical antipsychotic have been proposed [12-18].

Hence this one year prospective study has been undertaken to quantify the incidence of weight gain and hyperlipidemia due to atypical anti-psychotics, which may enhance physicians in their clinical decision making.

Objective

To determine treatment effects of atypical antipsychotics on weight and triglycerides in both schizophrenic and non-schizophrenic conditions in a community setting.

Method

Patients with schizophrenic and non –schizophrenic conditions were started randomly on atypical antipsychotics. Weight, BMI and triglycerides were measured every 3 months from the baseline for one year. There were 121 patients were enrolled in the study and 119 of them completed the one year follow up. There were 69 males and 50 females.

Treatment breakdown was as follows:

Olanzapine 51: risperidone 59: quetiapine 8: and Clozapine 1

The variables included in the analysis were

BMI- overweight is more than 25 to 29.9, Obesity is above 30

Hyperlipidemia is more than 1.7mmol/l.

Analysis and Interpretation

Descriptive and inferential analyses were carried out to examine the treatment effects on weight, BMI and triglycerides and in relationships to age, gender and disease. Clozapine was omitted from the analysis as there was only one patient.

The number of patients treated with Quetiapine is low compared to Olanzapine and Risperidone, yet, included as it is statistically viable,

but, this needs to be taken into consideration while interpreting the results. It should be noted that polypharmacy and ethnicity were not taken into consideration.

The study reveals that more males were treated with atypical anti-psychotics than females. Descriptive projection of drugs, age, gender and diagnosis can be seen in tables 1-4 & Figure 1. The age group under 19 years had been treated mostly with risperidone. A higher percentage of obesity 42.42% has been seen in schizophrenic patients and this validates the question of whether it is due to drugs or lifestyle or disease related. The mean weight gain more in females with risperidone , 7.57 kg SD 8.34 and more in females with olanzapine 4.71 kg SD 4.67.

The percentage of weight gain distribution seen more in males with risperidone 94.5% CI 79.87,99.10 than with Olanzapine 51.61% CI, 31.67 to 71.55 (Tables 5-11; Figures 2-5).

Weight gain more than 7% has been seen in males with risperidone 46% , with quetiapine 33% and with olanzapine 16% and

Table 1: Frequency distribution of antipsychotic drug use by gender.

Number of patients		
	F	M
Clozapine	1	0
Olanzapine	20	31
Quetiapine	5	3
Risperidone	22	37

Table 2: Frequency distribution of antipsychotic drug use by age-groups and drugs for gender combined.

Number of patients			
Age-groups	Olanzapine	Quetiapine	Risperidone
0-19	3	2	20
20-40	18	1	14
41-60	17	5	16
61+	13		9
Total	51	8	59

Table 3: Frequency (count and percentage) distribution of patients by diagnosis.

	Frequency	Percent
Attention Deficit Disorder (ADD)	17	14.29
Anxiety Disorder (Anx)	4	3.36
Behavioural Disorder (Beh)	2	1.68
Bipolar Disorder (Bipolar)	21	17.65
Mood Disorder (Mood)	23	19.33
Organic Brain Syndrome (OBS)	9	7.56
PDD	1	0.84
Schizophrenia (Schizo)	41	34.45
Schizophrenia With Diabetes (Schizo with Dia)	1	0.84
Total	119	100

Table 4: Mean age by drug and gender for all follow ups and age-groups.

	Female		Msale	
	Olanzapine	Risperidone	Olanzapine	Risperidone
Age	51	47	41	28

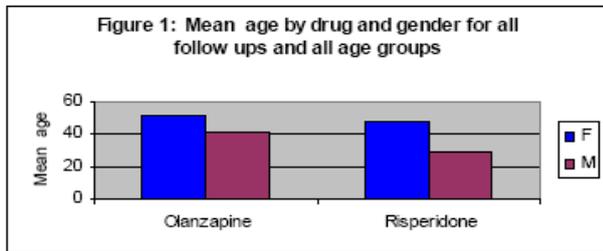


Figure 1: Mean age by drug and gender for all follow ups and all age groups.

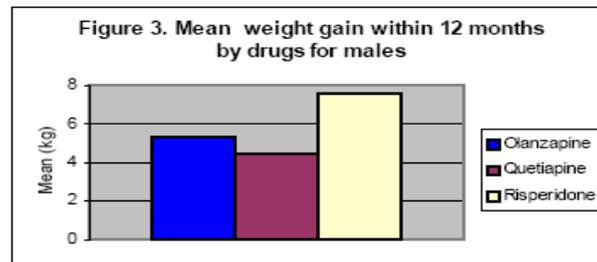


Figure 3: Mean weight gain within 12 months by drugs for males.

Table 5: Descriptive statistics of weight gain by drugs.

	Mean	Standard Deviation	Maximum
Olanzapine	5.02	4.57	18
Quetiapine	4.1	3.06	9.6
Risperidone	6.06	7.27	40.92

Table 7: Descriptive statistics of weight gain by drugs for females.

	Mean	Standard Deviation	Maximum
Olanzapine	4.71	4.67	18
Quetiapine	3.85	2.14	5.46
Risperidone	3.14	3.03	12.82

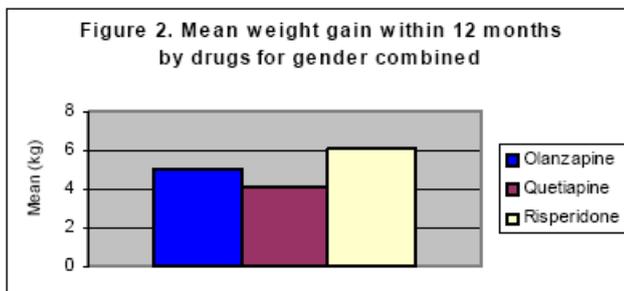


Figure 2: Mean weight gain within 12 months by drugs for gender combined.

Table 6: Descriptive statistics of weight gain by drugs for males.

	Mean	Standard Deviation	Maximum
Olanzapine	5.35	4.58	15.00
Quetiapine	4.43	4.57	9.60
Risperidone	7.57	8.34	40.92

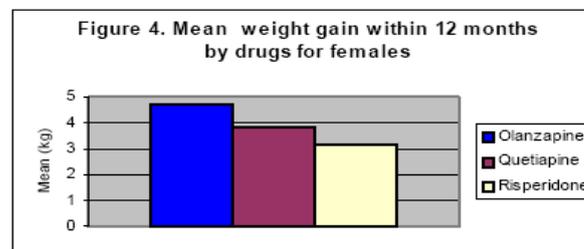


Figure 4: Mean weight gain within 12 months by drugs for females.

Table 8: Percentage distribution of weight gain by drugs.

	Weight gain	Lower CI	Upper CI
Olanzapine	64.71	50.29	79.13
Quetiapine	87.50	40.25	99.52
Risperidone	89.83	78.23	95.87

in females , quetiapine 40% ,with Olanzapine 35% and risperidone 9% (Tables 12-16; Figures 8-10).

Overweight range has been seen in males with quetiapine 100% , with olanzapine 58.06% and with risperidone 51.35% and in females with Quetiapine 90% , with Risperidone 51.35% and in females with Quetiapine 45% . OR is equal to 1.31%, 95% CI (.14,1.51 for gender

combined) (Tables 17-22; Figures 11-15).

Obesity range has been seen in males with quetiapine 33.33%, with Olanzapine 32.26% and with Risperidone 16.22% and with females with Risperidone 50% , olanzapine 20% and with Quetiapine 20% . OR is 1.12, 95%CI (-4.81 ,2.34).

It is interesting to note that the mean of triglycerides for males

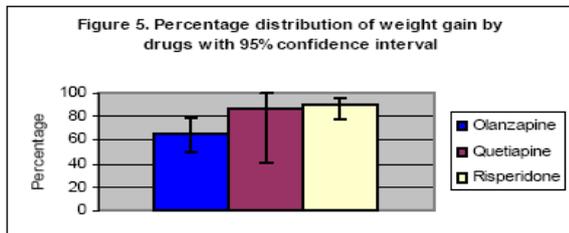


Figure 5: Percentage distribution of weight gain by drugs with 95% confidence interval.

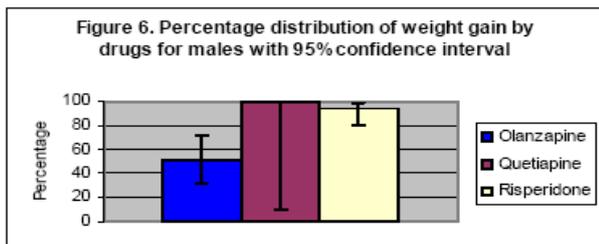


Figure 6: Percentage distribution of weight gain by drugs for males with 95% confidence interval.

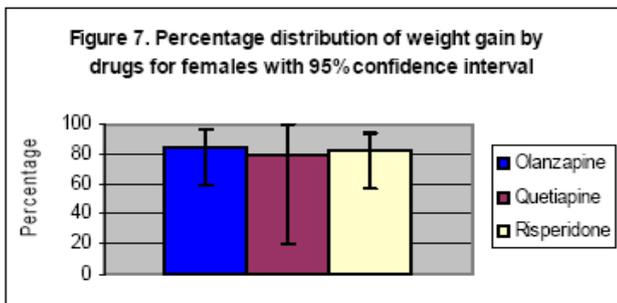


Figure 7: Percentage distribution of weight gain by drugs for females with 95% confidence interval.

Table 9: Significance testing of percentages of weight gain by drugs.

	Total in sample	Number with weight gain	Proportions with weight gain
Olanzapine	51	33	0.647
Quetiapine	8	7	0.875
Risperidone	59	53	0.898
Overall	118	93	0.788

pi	0.788
qi	0.212
$n1.(p1-p(total))^2$	1.015035402
$n2.(p2-p(total))^2$	0.060363401
$n3.(p3-p(total))^2$	0.716101695
Total	1.791500499
X2	10.72395184

Conclusion: The three proportions are significantly different at 0.01 level.

Table 10: Significance testing of percentages of weight gain by drugs for males.

	Total in sample	Number with weight gain	Proportions with weight gain
Olanzapine	31	16	0.516
Quetiapine	3	3	1.000
Risperidone	37	35	0.946
Overall	71	54	0.761

pi	0.761
qi	0.239
$n1.(p1-p(total))^2$	1.852192665
$n2.(p2-p(total))^2$	0.086917157
$n3.(p3-p(total))^2$	0.499235315
Total	2.438345137
X2	13.40641381s

Conclusion: The three proportions for males are significantly different at 0.01 level.

Table 11: Significance testing of percentages of weight gain by drugs for females.

	Total in sample	Number with weight gain	Proportions with weight gain
Olanzapine	20	17	0.850
Quetiapine	5	4	0.800
Risperidone	22	18	0.818
Overall	47	39	0.830

pi	0.83
qi	0.17
$n1.(p1-p(total))^2$	0.008171118
$n2.(p2-p(total))^2$	0.004436397
$n3.(p3-p(total))^2$	0.002963085
Total	0.0155706
X2	0.110351521

Conclusion: The three proportions for females are not significantly different at 0.01 level.

Table 12: Percent distribution of weight gain >7% within 12 months by drugs.

	Counts with weight gain > 7%	Total in sample	Percent
Olanzapine	12	51	0.24
Quetiapine	3	8	0.38
Risperidone	19	59	0.32
Total	34	118	0.29

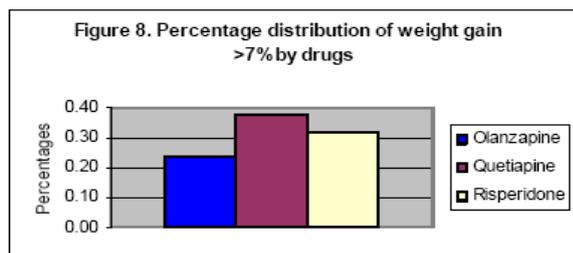


Figure 8: Percentage distribution of weight gain >7% by drugs.

Table 13: Percent distribution of weight gain >7% within 12 months by drugs for males.

	Counts with weight gain > 7%	Total in sample	Percent
Olanzapine	5	31	0.16
Quetiapine	1	3	0.33
Risperidone	17	37	0.46

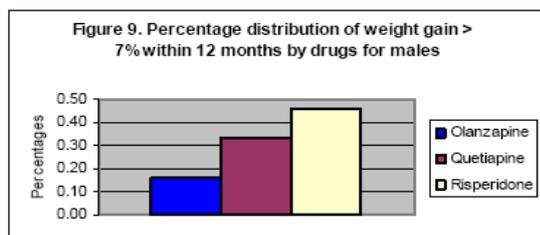


Figure 9: Percentage distribution of weight gain >7% with 12 months by drugs for males.

Table 14: Percent distribution of weight gain >7% within 12 months by drugs for females.

	Counts with weight gain > 7%	Total in sample	Percent
Olanzapine	7	20	0.35
Quetiapine	2	5	0.40
Risperidone	2	22	0.09

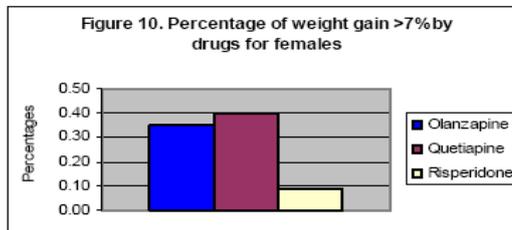


Figure 10: Percentage of weight gain >7% by drugs for females.

Table 15: For gender combined.

	Total in sample	Number with weight gain > 7%	Number with weight gain <=7%	Proportions with weight gain > 7%
Olanzapine	51	12	39	0.235
Quetiapine	8	3	5	0.375
Risperidone	59	19	40	0.322
Overall	118	34	84	0.288

pi	0.288135593
qi	0.711864407
n1.*(p1-p(total))^2	2.823529412
n2.*(p2-p(total))^2	1.125
n3.*(p3-p(total))^2	6.118644068
Total	10.06717348
X2	49.08099563

Conclusion: The three proportions for gender combined are significantly different at 0.01 level.

Table 16: For male.

	Total in sample	Number with weight gain > 7%	Number with weight gain <=7%	Proportions with weight gain > 7%
Olanzapine	31	5	26	0.161
Quetiapine	3	1	2	0.333
Risperidone	37	17	20	0.459
Overall	71	23	48	0.324

pi	0.761
qi	0.239
n1.*(p1-p(total))^2	0.806451613
n2.*(p2-p(total))^2	0.333333333
n3.*(p3-p(total))^2	7.810810811
Total	8.950595757
X2	49.21181531

Conclusion: The three proportions for males are significantly different at 0.01 level.

Table 17: Mean BMI by drugs and gender for all age-groups and all follow-ups.

	Olanzapine	Quetiapine
F	25.22	30.31
M	28.24	25.88

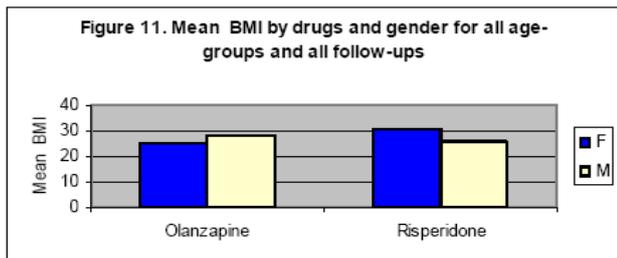


Figure 11: Mean BMI by drugs and gender for all age groups and all follow-ups.

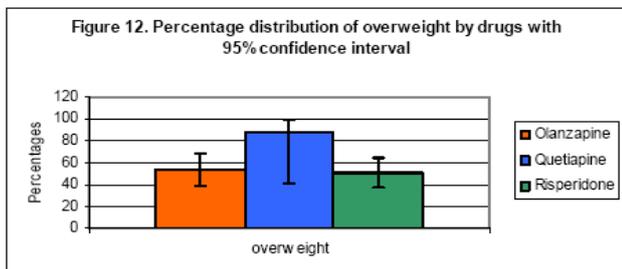


Figure 12: Percentage distribution of overweight by drugs with 95% confidence interval.

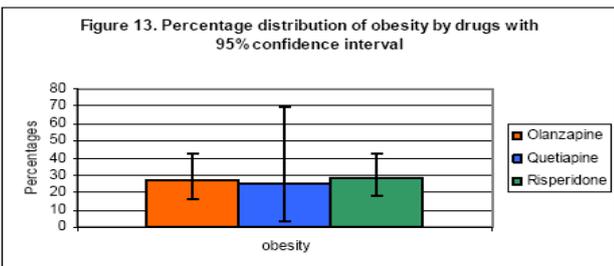


Figure 13: Percentage distribution of obesity by drugs with 95% confidence interval.

Table 18: Percentage distribution of overweight and obesity by drugs and gender.

		Overweight	obesity
Olanzapine	F	45	20
	M	58.06	32.26
Quetiapine	F	80	20
	M	100	33.33
Risperidone	F	50	50
	M	51.35	16.22

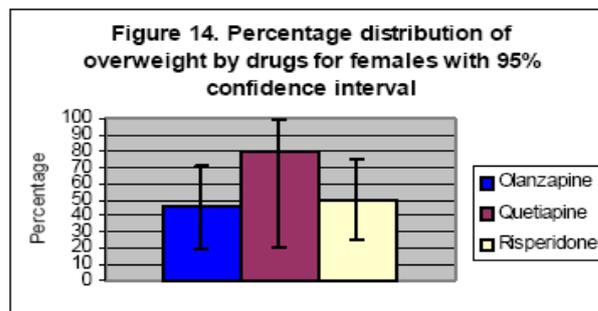


Figure 14: Percentage distribution of overweight by drugs for females with 95% confidence interval.

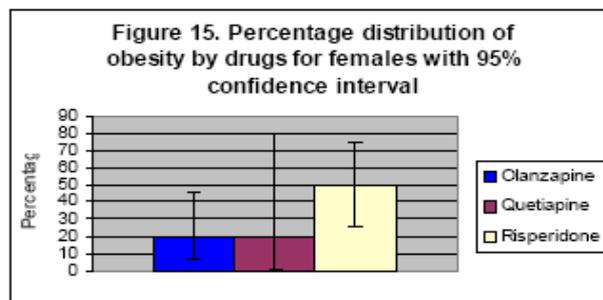


Figure 15: Percentage distribution of obesity by drugs for females with 95% confidence interval.

Table 19: Significance testing of percentages of overweight by drugs.

	Total in sample	Number with over weight	Proportions with over weight
Olanzapine	51	27	0.529
Quetiapine	8	7	0.875
Risperidone	59	30	0.508
Overall	118	64	0.542

pi	0.542
qi	0.457627119
$n1 \cdot (p1-p(\text{total}))^2$	0.008567518
$n2 \cdot (p2-p(\text{total}))^2$	0.8851264
$n3 \cdot (p3-p(\text{total}))^2$	0.06779661
Total	0.961490528
X2	3.87378302

Conclusion: The three proportions are not significantly different at 0.01 level.

Table 20: Significance testing of percentages of overweight by drugs for females.

	Total in sample	Number with over weight	Proportions with over weight
Olanzapine	20	9	0.450
Quetiapine	5	4	0.800
Risperidone	22	11	0.500
Overall	47	24	0.511

pi	0.510638298
qi	0.489361702
$n1 \cdot (p1-p(\text{total}))^2$	0.073540063
$n2 \cdot (p2-p(\text{total}))^2$	0.418650973
$n3 \cdot (p3-p(\text{total}))^2$	0.002489814
Total	0.494680851
X2	1.979619565

Conclusion: The three proportions for females are not significantly different at 0.01 level.

Table 21: Significance testing of percentages of obesity by drugs.

	Total in sample	Number with obesity	Proportions with obesity
Olanzapine	51	14	0.275
Quetiapine	8	2	0.250
Risperidone	59	17	0.288
Overall	118	33	0.280

pi	0.280
qi	0.720338983
$n1 \cdot (p1-p(\text{total}))^2$	3.659282041
$n2 \cdot (p2-p(\text{total}))^2$	0.683855214
$n3 \cdot (p3-p(\text{total}))^2$	3.813559322
Total	8.156696577
X2	40.48978365

Conclusion: The three proportions are significantly different at 0.01 level.

Table 22: Significance testing of percentages of obesity by drugs for males.

	Total in sample	Number with obesity	Proportions with obesity
Olanzapine	31	10	0.323
Quetiapine	3	1	0.333
Risperidone	37	6	0.162
Overall	71	17	0.239

pi	0.239
qi	0.76056338
$n1 \cdot (p1-p(\text{total}))^2$	1.797518414
$n2 \cdot (p2-p(\text{total}))^2$	0.094311151
$n3 \cdot (p3-p(\text{total}))^2$	4.493117835
Total	6.3849474
X2	35.06156846

Conclusion: The three proportions for males are significantly different at 0.01 level.

Table 23: Mean triglycerides by drugs and age-groups for gender combined and all follow ups.

	0-19	20-40	41-60	61+
Olanzapine	1.49	1.70	1.76	2.07
Risperidone	1.07	3.03	2.00	1.57

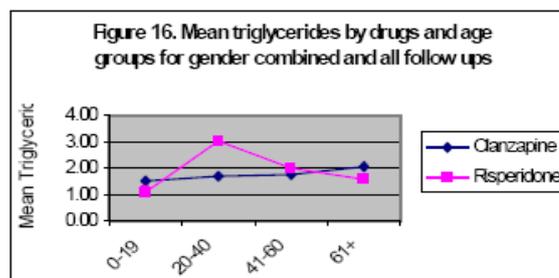


Figure 16: Mean triglycerides by drugs and age groups for gender combined and all follow ups.

Table 24: Percentage distribution of dyslipidemia by gender and groups.

	F	M
Olanzapine	65	54.84
Quetiapine	80	33.33
Risperidone	45.45	43.24

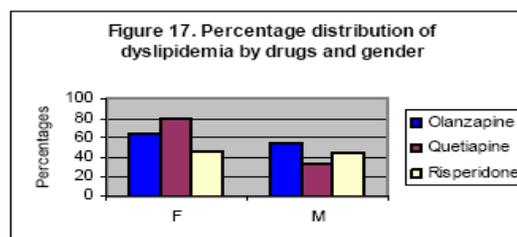


Figure 17: Percentage distribution of dyslipidemia by drugs and dender.

with Risperidone 1.92 > Olanzapine 1.7 and in female Olanzapine 1.97> Risperidone 1.78 and this correlates with the observed weight gain pattern as shown above (Tables 23-28; Figures16-19).

The percentage of hyper lipidemia for males with Olanzapine 54.84%> Risperidone 43.24% > Quetiapine 33.33% and for females Quetiapine 80%> Olanzapine 65% > Risperidone 45.45%.

Age related incidence

The highest incidence of hyperlipidemia seen between the age group of 20 to 40 years with Risperidone and for Olanzapine it has been evidenced in the age group of 61 +.

It is evidenced higher incidence of weight gain and hyperlipidemia in schizophrenia and bipolar disorder compared to other conditions (Tables 29-32; Figures 20-23).

The Odd Ratio for hyperlipidemia with Olanzapine Vs Risperidone is 1.81(SE (O) .77034827)

Discussion

This is the only study, to the author’s knowledge which examined the effects of treatment with, atypical anti psychotics in both schizophrenic and non-schizophrenic patients in a non- academic community setting and attempted to examine the effects in relation to age, gender and disease.

The study reveals alterations in weight seen from the baseline in all three atypical anti-psychotics but showing a differential trend in relation to age, gender and disease. It shows that males gain more weight with risperidone and females gain more weight with Olanzapine.

It is also evidenced that all three drugs induce hyperlipidemia in varying degree, but, showing a differential trend in relation to age, gender and disease.

One could see that male seems to be having more propensities with Risperidone and female with Olanzapine and similar pattern is shown with the weight gain. This reveals probable correlation exists between weight gain and hyperlipidemia.

In terms of age, it is quite interesting to note that the highest propensity for hyper lipidemia is seen in the age group of 20 to 40 years with Risperidone and Quetiapine, whereas, the highest incidence seen in the age group of 61 years plus with Olanzapine. This may signify importance in the clinical scenario and may enhance physicians decision making in their clinical management enlightening the need to do close monitoring when they prescribe either of the atypical for any particular gender or the age group.

Conclusion

This is the first study to the author’s knowledge revealing varying effects with atypical anti-psychotics treatment on weight, and triglycerides and in relationship to age, gender and disease.

It is evidenced in this prospective study that atypical antipsychotics do affect weight, BMI and triglycerides at varying degrees and there is no conclusive explanation to date of these effects attributed solely to the pharmacodynamic profile of the drugs.

It may be beneficial to be cognizant of these adverse varying effects

Table 25: Percentage distribution of dyslipidemia by drugs.

	Dyslipidemia	Lower CI	Upper CI
Olanzapine	58.82	43.99	73.65
Quetiapine	62.5	21.75	91.75
Risperidone	44.07	30.28	57.86

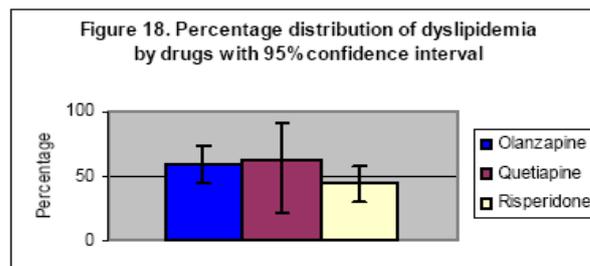


Figure 18: Percentage distribution of dyslipidemia by drugs with 95% confidence interval.

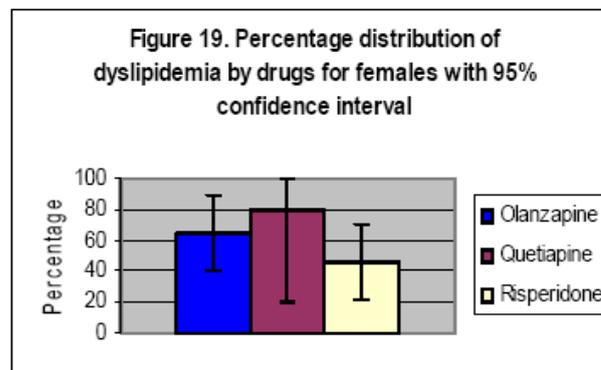


Figure 19: Percentage distribution of dyslipidemia by drugs for females with 95% confidence interval.

Table 26: Significance testing of percentages of dyslipidemia by drugs for males.

	Total in sample	Number with dyslipidemia	Proportions with dyslipidemia
Olanzapine	31	17	0.548
Quetiapine	3	1	0.333
Risperidone	37	16	0.432
Overall	71	34	0.479

pi	0.479
qi	0.521126761
n1.*(p1-p(total))^2	0.149797467
n2.*(p2-p(total))^2	0.174437906
n3.*(p3-p(total))^2	0.746442685
Total	1.070678058
X2	4.290372091

Conclusion: The three proportions for males are not significantly different at 0.01 level.

Table 27: Significance testing of percentages of dyslipidemia by drugs for females.

	Total in sample	Number with dyslipidemia	Proportions with dyslipidemia
Olanzapine	20	13	0.650
Quetiapine	5	4	0.800
Risperidone	22	10	0.455
Overall	47	27	0.574

pi	0.574
qi	0.425531915
$n1 \cdot (p1 - p(\text{total}))^2$	0.114101403
$n2 \cdot (p2 - p(\text{total}))^2$	0.254323223
$n3 \cdot (p3 - p(\text{total}))^2$	0.316391621
Total	0.684816248
X2	2.801405724

Conclusion: The three proportions for females are not significantly different at 0.01 level.

Table 28: Mean triglycerides by drug and gender for all follow ups and all age groups.

F		M	
Olanzapine	Risperidone	Olanzapine	Risperidone
1.97	1.78	1.70	1.92

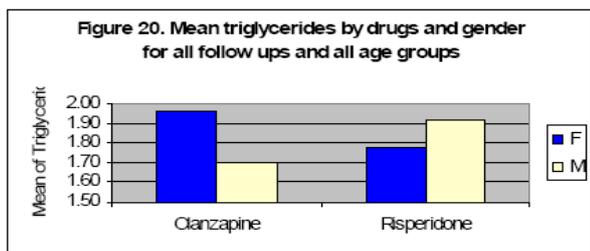


Figure 20: Mean triglycerides by drugs and gender for all follow ups and all age groups.

Table 29: Mean triglycerides by drugs and follow ups for gender combined and all age groups.

	3 Months	6 Months	9 Months	12 Months
Olanzapine	1.79	1.75	1.87	1.82
Risperidone	1.95	2.00	1.76	1.76

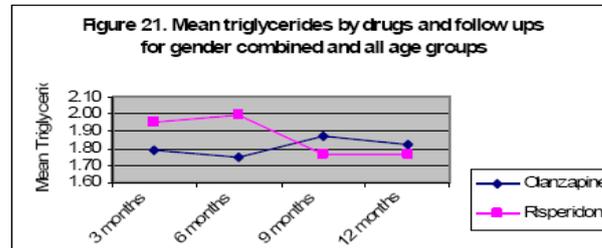


Figure 21: Mean triglycerides by drugs and follow ups fro gender combined and all age groups.

Table 30: Mean triglycerides by drugs and follow ups for males and all age groups.

	3 Months	6 Months	9 Months	12 Months
Olanzapine	1.64	1.62	1.78	1.77
Risperidone	1.94	2.14	1.82	1.77

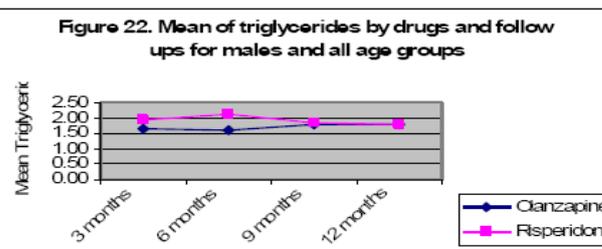


Figure 22: Mean of triglycerides by drugs and follow ups for male and all age groups.

Table 31: Mean triglycerides by follow ups and drugs for females and all age groups.

	3 Months	6 Months	9 Months	12 Months
Olanzapine	2.02	1.95	2.00	1.90
Risperidone	1.98	1.76	1.67	1.74

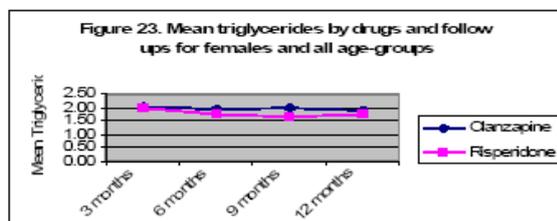


Figure 23: Mean triglycerides by drugs and follow ups for females and all age-groups.

Table 32: The standard error is used to gauge the precision of the estimated odds ratio. OR represents Odds Ratio. s.e.(o) represents standard error of the odds ratio.

	dyslipidemia	Normal triglycerides
Olanzapine	30	21
Risperidone	26	33
OR	1.81	
s.e.(o)	0.70034827	

of the drugs, in relation to age, gender and disease which may induce metabolic or cardiovascular morbidities. It is prudent to advocate individual close monitoring with ongoing education on life style, diet, and exercise rather discriminating the drugs with heightened risk and discarding their clinical efficacy in various psychiatric conditions.

In every clinical management, it is the benefit and risk discretion values the judgment and this valued clinical prudence advocates the wisdom of heuristic attitude in following up the patients on atypical antipsychotics, on an individual basis.

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