IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 2 Ser.12 (February. 2020), PP 34-43
www.iosrjournals.org

Effect of Modified Electroconvulsive Therapy on Blood Glucose and Lipid Profile and Its Prediction on Response in Psychotic Mania

Dr. Budhayan Roy[1], Dr. D. Ram[2], Dr. Nishant Goyal[3]
(Department of Psychiatry, Central Institute of Psychiatry, Ranchi, Jharkhand)

Abstract:
Background :*Electroconvulsive therapy is considered to be highly efficacious in BPAD in terms of remission or marked clinical improvement has been reported to be about 80% (Mukherjee et al., 1995). There are controversies regarding the mechanism of action, and exact mechanism is not proved beyond doubt. One hypothetical mechanism to explain the effectiveness of ECT is that ECT is an acute stress reaction. It invokes changes in the activity of the different hormone levels in the body. This in turn alters the metabolism of substrates in the body. This hormonal changes affects biochemical parameters, including blood sugar & lipid profile in human body.*
Materials and Methods: *Patients meeting the inclusion and exclusion criteria was evaluated on socio-demographic and clinical data sheet. The study group was evaluated on YMRS, CGI, BPRS, Modified overt aggression scale at baseline and on every alternate day after each session of Modified ECT up to 50% improvement in YMRS scale. Modified ECT was given; After 12 hours of fasting, 10ml of venous blood using all aseptic precaution was collected from study group before first Modified ECT, 20 minutes after first Modified ECT and 24hrs after the first modified ECT. These blood samples was evaluated for fasting blood glucose and lipid profile on the same day at the institute's biochemistry laboratory. Subjects in control group was evaluated for relevant socio-demographic and clinical data..*
Subjects in the control group was screened with General Health Questionnaire (GHQ-12) ; only those with scores less than or equal to 3 was included. 10ml of venous blood using all aseptic precaution was collected from control group only once at 9:00 AM after 12 hours of fasting and was subjected for fasting blood sugar and lipid profile.
Results: *There was significant difference between cases and controls in cholesterol (p=.000) and LDL (p=.000) with normal control have higher cholesterol and LDL. There was significant increase in fasting blood sugar between baseline sample (1st sample) and 20 minutes after first modified ECT sample (2nd sample), but no significant difference between baseline and 24 hours after first modified ECT sample (3rd sample). Regarding cholesterol, triglyceride, HDL, LDL and VLDL there was no significant difference between 1st sample, 2nd sample and 3rd sample. Significant correlation is seen between BPRS at baseline & baseline FBS (p = .019), between CGIS at baseline & baseline triglyceride (p= .037) & between CGIS at baseline & baseline VLDL (p= .028) of patient group. No significant improvement between blood sugar increase and symptom improvement in YMRS, BPRS, MOAS, CGIS (illness severity) scales.*
Conclusion: *The current study demonstrates the presence of statistically significantly lower cholesterol and LDL level in study group. Also, this study explored that ECT increases blood sugar immediately, but the rise is not sustained and this rise in blood sugar have no correlation with symptom improvement in bipolar mania. This is a novel finding because the earlier studies didn't measure whether the rise is sustained and it have any correlation with symptom improvement or not.*
Key Word*: Modified ECT, Blood sugar, Lipid profile.*

Date of Submission: 03-02-2020 Date of Acceptance: 18-02-2020

I. Introduction

Mood disorder consists of group of psychiatric disorder, where mood is pathological and a related psychomotor disturbance dominants the entire clinical picture. Mood disorder can be conceptualised as a constellation of sign and symptoms that persists for weeks to months and recurs periodically. There has been debate between two different school of thoughts. According to Aubrey Lewis and his followers from Maudsley school, the mood disorder is explained as a continuum model, that starts from anxiety disorder to mild depression to severe endogenous and psychotic depression. On the other hand, the Newcastle school, led by Martin Roth believes that these disorders are demarcated from each other. Bipolar disorders (BPD) are major, life-long psychiatric illnesses found in 2–5% of the population. Prognosis for BPD was earlier considered

relatively favourable, but contemporary findings suggest that disability and poor outcomes are prevalent, despite major therapeutic advances (Mukherjee et al., 1995). Many cases of bipolar affective disorder do not improve on just pharmacology and requires additional intervention like Electroconvulsive Therapy (ECT). Also, the adverse effect of the drugs adds to the burden of the disease. ECT also forms the first line treatment of BPAD mania. Efficacy of ECT in manic phase in terms of remission or marked clinical improvement has been reported to be about 80% (Mukherjee et al., 1995). It is also reported to be equally or more efficacious than psychotropic medications (Mukherjee and Debsikdar, 1992; Sikdar et al., 1994; Thomas and Reddy, 1982). With improving methods in ECT the adverse effect of conventional ECT has significantly reduced. Though extensionally used in various psychiatric disorders, mechanism of action of ECT is still under study. Though many hypothesis have been proposed by various authors, area still remains under covered. Most commonly the explanations are focused on the messenger molecules, or neurotransmitters, that pass from one neuron to another. Among the more notable of these molecules are dopamine, serotonin, norepinephrine and gamma amino- butyric acid (GABA)—neurotransmitters that are typically central to biologically based theories of mental illness. Each of these molecules binds to specific receptors on neuronal-cell surfaces and in turn modifies the activity of these neurons. Psychotropic medicines alter the concentrations of these neurotransmitters and so modify the activity of neurons in certain parts of the brain, most notably those areas believed to play important roles in mental disorders (Fink, 2000). One hypothetical mechanism to explain the effectiveness of ECT is that ECT is an acute stress reaction and it invokes changes in the activity of the different hormone levels in the body, which in turn alters the metabolism of substrates in the body. This hormonal changes affects blood sugar & lipid profile in human body.

Earlier studies have found contradictory results of effect of ECT on blood sugar and lipid profile. A few studies have found that blood sugar level immediately rises after ECT, while some studies have refuted this inference. But these researches didn't observed that whether the blood sugar rise was sustained or not. Studies also didn't look into whether these changes in blood sugar was associated with better response with ECT or not. Studies also shows that blood cholesterol level also rises after ECT, but it have no impact on triglyceride level, HDL, LDL level (Ghanizadeh et al., 2012). So the current study is needed to observe the immediate as well as sustained change of blood sugar and lipid profile, 20 minutes & 24 hours after ECT, and also to investigate the correlation of blood parameters change after ECT with degree of response on ECT.

II. Material And Methods

Study design: open label study
Sample size: The study group comprises of 30 patients diagnosed as Mania with psychotic symptoms and Bipolar affective disorder, current episode manic with psychotic symptoms and 30 age & sex matched control.
Sampling technique: Purposive
Venue: Central Institute of Psychiatry, Kanke, Ranchi
Duration: subjects were recruited between June, 2016 to January, 2017

INCLUSION CRITERIA FOR STUDY GROUP

1. Patients fulfilling the criteria for ICD-10 (WHO-1993) for Mania with psychotic symptoms and Bipolar affective disorder current episode mania with psychotic symptoms.
2. Patient of male sex aged between 18 to 60 years
3. Patients who received a course of ECT.
4. Those who gave informed consent.

EXCLUSION CRITERIA FOR STUDY GROUP

1. Patients who fulfilled criteria for any other mental disorder other than Mania with psychotic symptoms or Bipolar affective disorder current episode mania with psychotic symptoms.
2. Age below 18yrs and above 60yrs and female sex.
3. Patient who received second generation oral or depot antipsychotic for last three month.
4. Patients diagnosed as suffering from diabetes mellitus, dyslipidemia or other major medical/neurological disorder by history or examination or investigation.
5. Patients who took drugs causes derangement in lipid profile or blood sugar level.
6. Patient who had substance in dependence pattern.

INCLUSION CRITERIA FOR CONTROL GROUP

1. Age & education matched to study groups.
2. Male sex.
3. GHQ 12 score <=3 (Goldberg and Williams, 1998).
4. Those who gave written informed consent.

EXCLUSION CRITERIA FOR CONTROL GROUP

1. History of any psychiatric disorder.
2. Female sex.
3. Any major neurological or medical illness (including head injury and epilepsy).
4. No Drug or substance dependence, except nicotine or caffeine use.

TOOLS USED IN THE COLLECTION OF DATA

1. Sociodemographic and clinical data sheet.
2. ECT machine.
3. Young's Mania Rating Scale (Young et al., 1978).
4. Brief Psychiatric Rating Scale (Hedlund, 1980).
5. Modified Overt Aggression Scale (Ratey et al., 1991).
6. Clinical Global Impression- Severity Scale (Spearing et al., 1997).
7. General Health Questionnaire (GHQ-12) (Goldberg and Williams, 1998).
8. Blood from study and control group for evaluation of fasting blood sugar and lipid profile.

DESCRIPTION OF TOOLS

1. Socio demographic data sheet containing the variables—serial number, case record file number, date of admission, name, father's name, residence, age at admission (in years), sex, religion, education, occupation before admission, economic status, marital status, type of family, habitat, no of children. The clinical data sheet consists of chief complaints, onset, course, progress, history of present illness, treatment history, past history of psychiatry/ medical illness, history of any endocrinal disorder, family history of any psychiatric/ medical Illness, personal history, premorbid personality, physical examination, mental status examination, diagnosis (ICD-10).
2. ECT machine- Ultra Brief pulse (The Spectrum 5000Q, MECTA Corporation). In the Ultra Brief pulse the dosing parameter used is 0.3 ms pulse width, with a fixed current of 800 mA.
3. Young's Mania Rating Scale (Young et al., 1978): 11-item clinician-rated scale designed to assess severity of manic symptoms. Four of the YMRS items are rated on a 0–8 scale, with the remaining 5 items being rated on a 0–4 scale.A score of ≤12 indicates remission of symptoms. First item – Elevated mood, is rated, absent as 0, mildly or possibly increased on questioning as 1, definite subjective elevation: optimistic, self-confident; cheerful; appropriate to content as 2, elevated, inappropriate to content; humorous as 3, euphoric, inappropriate laughter singing as 4. Second item - Increased motor activity-energy, is rated, absent as 0, subjectively increased as 1, animated; gestures increased as 2, excessive energy; hyperactive at times; restless (can be calmed) as 3, motor excitement continues hyperactivity (cannot be calmed) as 4. Third item - Sexual interest, rated absent as 0, mildly or possibly increased as 1, definite subjective increase on questioning as 2, spontaneous sexual content; elaborates on sexual matters; hypersexual by self-report as 3, overt sexual acts (toward subjects, staff, or interviewer) as 4. Fourth item – sleep, is rated, no decrease in sleep as 0, sleeping less than normal amount by up to one hour as 1, sleeping less than normal by more than one hour as 2, reports decreased need for sleep as 3, denies need for sleep as 4. Fifth item – irritability, is rated, absent as 0, subjectively increased as 2, irritable at times during interview; recent episodes of anger or annoyance on ward as 4, frequently irritable during interview; short, curt throughout as 6, hostile, uncooperative; interview impossible as 8. Sixth item - Speech (rate and amount), rated absent as 0, feels talkative as 2, increased rate or amount at times, verbose at times as 4, push; consistently increased rate and amount; difficult to interpret as 6, Pressured; uninterruptible; continuous speech as 8. Seventh item - Language-thought disorder, is rated absent as 0, circumstantial; mild distractibility; quick thoughts as 1, distractible; loses goal of thought; changes topics frequently; racing thoughts as 2, flight of ideas; tangentiality; difficult to follow; rhyming; echolalia as 3, Incoherent; communication impossible as 4. Eighth item – content, is rated normal as 0, questionable plans, new interests as 2, special project(s); hyper religious as 4, grandiose or paranoid ideas; ideas of reference as 6, delusions; hallucinations as 8, Ninth item - Disruptive-aggressive behavior is rated absent, cooperative as 0, sarcastic; loud at times, guarded as 2, demanding; threats on ward as 4, threatens interviewer shouting; interview difficult as 6, assaultive; destructive; interview impossible as 8. Tenth item – Appearance is rated appropriate dress and grooming as 0, minimally unkempt as 1, poorly groomed; moderately disheveled; overdressed as 2, disheveled; partly clothed; garish make-up as 3, completely unkempt; decorated; bizarre garb as 4. Eleventh item – Insight , is rated, if present; admits illness; agrees with need for treatment as 0, possibly ill as 1, admits behavior change, but denies illness as 2, admits possible change in behavior, but denies illness as 3, denies any behavior change as 4.
4. Brief Psychiatric Rating Scale (Hedlund, 1980): The Brief Psychiatric Rating Scale (BPRS) is rating scale which a clinician or researcher may use to measure psychiatric symptoms such as depression, anxiety, hallucinations and unusual behavior. Each symptom is rated 1-7 and total of 18 symptoms are scored. The items are, somatic concern, anxiety, emotional withdrawal, conceptual disorganization, guilt feeling, tension, mannerism and posturing, grandiosity, depressive mood, hostility, suspiciousness, hallucinatory

behavior, motor retardation, uncooperativeness, unusual thought content, blunted affect, excitement, disorientation. These items are rated as, not assessed-0, not present-1, very mild-2, mild-3, moderate-4, moderately severe-5, severe-6, extremely severe-7.

5. Modified Overt Aggression Scale (Ratey et al., 1991): The Modified Overt Aggression Scale (MOAS) is a four part behavior rating scale designed to measure four types of aggressive behavior as witnessed in the past week. Each section consists of five questions, with the first section regarding verbal aggression, rated as no verbal aggression as 0, shouts angrily, curses mildly or makes personal insult as 1, curses viciously, is severely insulting, has temper outbursts as 2, impulsively threatens, violence towards others and self as 3, threatens violence towards others or self, repeatedly or deliberately as 4. The second section focusing on aggression against property, rated No aggression against property as 0, slams door, rips clothing, urinates on floor as 1, throws objects down, kicks furniture, defaces wall as 2, breaks objects, smashes windows as 3, Sets fire, throws objects dangerously as 4. The third section measuring auto-aggression, rated No auto aggression as 0, pricks or scratches skin, pulls hair out, hits self (without injury) as 1, bangs head, hits fists into wall, throws self into floor as 2, inflicts minor cuts, bruises , burns or welts on self as 3, inflicts major injury on self or makes a suicidal attempt as 4. The fourth section concerning physical aggression rated no physical aggression as 0, makes menacing gestures, swings at people, grabs at clothing as 1, strikes, pushes, scratches, pulls hairs of others (without injury) as 2, attacks others causing mild injury (bruises, sprains, welts etc.) as 3, attacks others causing serious injury as 4. Verbal aggression score multiplied with 1, aggression against property score multiplied with 2, auto aggression score multiplied with 3, physical aggression score multiplied with 4. Total score is added. Respondents are asked to check whether each statement describes the child's behavior over the previous week.

6. Clinical Global Impression- Severity Scale (Spearing et al., 1997) : The Clinical Global Impression – Severity scale (CGI-S) is a 7-points scale that requires the clinician to rate the severity of the patient's illness at the time of assessment, relative to the clinician's objective assessment with patients who have the same diagnosis and global improvement. Severity of illness is rated as Not assessed as 0, Normal not at all ill as 1, Borderline mentally ill as 2, Mildly ill as 3, Moderately ill as 4, Markedly ill as 5, Severely ill as 6, Among the most extremely ill patients as 7. Global improvement rated as Not assessed as 0, Very much improved as 1, Much improved as 2, Minimally improved as 3, No change as 4, Minimally worse as 5, Much worse as 6, Very much worse as 7.

7. General Health Questionnaire (GHQ-12) (Goldberg and Williams, 1998): It is a self-report questionnaire to screen for any psychiatric morbidity. In the present study 12-item version is to be used. Here 12 questions are asked. Questions are whether the patient recently been able to concentrate on whatever he/she is doing? Whether he/she recently lost much sleep over worry? Whether he/she recently felt to be playing a useful part in things? Whether he/she recently felt capable of making decisions about things? Did the patient recently felt constantly under strain? Did the patient recently felt he/she could not overcome difficulties? Did the patient recently been able to enjoy normal day-to-day activities? Whether he/she recently been able to face up problem? Whether the patient recently been feeling unhappy and depressed? Had the patient recently been losing confidence? Had the patient recently been thinking himself/herself as a worthless person? Had he/she recently been feeling reasonable happy all things considered? Answers are usually rated better than usual, same as usual, less than usual or much less than usual as 1, 2, 3, 4 respectively & total score is added up. If total score is <= 3 then the subject will be included in control group.

PROCEDURE

The study was doneat a tertiary care hospital Central Institute of Psychiatry, Ranchi, catering primarily to a population from the eastern part of India. The study subjects were recruited between June, 2016 to January, 2017. There were no drop-outs in the study. Patients meeting the inclusion and exclusion criteria devised in present study was evaluated on sociodemographic and clinical data sheet. The study group was evaluated on YMRS, CGI, BPRS, Modified overt aggression scale at baseline and on every alternate day after each session of Modified ECT up to 50% improvement in YMRS scale. Modified ECT was given using atropine/ glycopyrrolate, ondansetron/ metoclopramide, succinyle choline, thiopentone/ propofol. After 12 hours of fasting, 10ml of venous blood using all aseptic precaution was collected from study group before first Modified ECT, 20 minutes after first Modified ECT and 24hrs after the first modified ECT. These blood samples was evaluated for fasting blood glucose and lipid profile on the same day at the institute's biochemistry laboratory. Fasting blood sugar was measured by hexokinase method and lipid profile measured by enzyme coupled reaction. The subjects included in the study group received Modified ECT treatment and 1st generation antipsychotic with or without mood stabilizer. The number of Modified ECT patient receives was determined by the treating unit. The dose of medications was also determined by the treating unit and was recorded during each step of procedure. Subjects in control group was recruited from the hospital staff and community living in the vicinity of CIP. Written informed consent was taken after explaining the procedure in detail. Relevant socio-demographic and clinical data was collected from all the participants. Subjects in the control groupwas screened

with General Health Questionnaire (GHQ-12) (Goldberg and William, 1998); only those with scores less than or equal to 3 was included. 10ml of venous blood using all aseptic precaution was collected from control group only once at 9:00 AM after 12 hours of fasting and was subjected for fasting blood sugar and lipid profile.

STATISTICS

Statistical analysis was done using IBM SPSS version 23.0. The entire socio-demographic and clinical characteristics for continuous variables were compared using the student t-test. For categorical variables, chi-square/fisher's exact test were used. Comparison has been made between baseline blood parameters (fasting blood sugar, cholesterol, triglyceride, HDL, LDL, VLDL) of 30 patients and 30 normal healthy controls using t-test.

Comparison between three samples (fasting blood sugar, cholesterol, triglyceride, HDL, LDL, VLDL taken just before ECT, 20 minutes & 24 hours after ECT) of 30 cases were made using one way Anova and Post Hoc Bonferroni test. Correlation between baseline blood parameters and baseline scores of YMRS, BPRS, MOAS and CGIS of 30 cases is seen using Pearson's correlation.

Change in fasting blood sugar between 1st sample (taken at baseline) and 2nd sample (20 min after 1st ECT) is correlated with the number of ECT sessions needed for 50% reduction in YMRS scales and reduction in YMRS, BPRS, MOAS, CGIS (illness severity) scales after 1st ECT, from baseline and score in CGII (global improvement) after 1st ECT. Pearson's correlation was used for correlation.

III. Result

GENERAL CONSIDERATION

This study was conducted at Central Institute of Psychiatry (CIP), Ranchi. 30 individuals who fulfilled the inclusion criteria for study group and diagnostic criteria for of either mania with psychotic symptoms (F 30.2) or bipolar affective disorder current episode manic with psychotic symptoms (F31.2), made according to the International Classification of Diseases-10 - DCR (WHO, 1993) were recruited for the study group and 30 normal control who fulfilled the inclusion criteria for normal control group were recruited for the control group. It was a randomized controlled hospital based study, in which the subjects were recruited by purposive sampling technique.

TABLE 1: COMPARISION OF SOCIO-DEMOGRAPHIC VARIABLE (CATEGORICAL) BETWEEN PATIENT GROUP OF BIPOLAR MANIA WITH ECT AND CONTROL GROUP [N=60]

Variable		Patient Group, N=30, N(%)	Control Group, N=30, N(%)	X^2/t	df	P
Religion	Hindu	20 (66.7 %)	25 (83.3 %)	2.22	1	.136
	Other	10 (33.3 %)	5 (16.7 %)			
Residence	Urban	26 (86.7 %)	30 (100 %)	45.882	1	**.000*** **
	Rural	4 (13.3 %)	0 (0 %)			
Education	Upto 6th Class	6 (20 %)	0 (0 %)	48.778[f]	2	**.000*** **
	7th – 12th Class	23 (76.7 %)	2 (6.7 %)			
	Graduate Or More	1 (3.3 %)	28 (93.3 %)			
Occupation	Employed	24 (80 %)	30 (100 %)	6.667[f]	1	**.024***
	Unemployed	6 (20 %)	0 (0 %)			
Marital Status	Married	14 (46.7 %)	7 (23.3 %)	3.590	1	.058
	Unmarried	16 (53.3 %)	23 (76.6 %)			
Family Income	<12000 Rs/m	26 (86.7 %)	10 (33.3 %)	17.778	1	**.000*** **
	>12000 Rs/m	4 (13.3 %)	20 (66.7 %)			
Past History	Absent	6 (20 %)	30 (100 %)	40.000	1	**.000*** **
	Present	24 (80 %)	0 (0 %)			
Family History	Absent	19 (63.3 %)	30 (100 %)	13.469	1	**.000*** **
	Present	11 (36.7 %)	0 (0 %)			
Treatment History	Absent	7 (23.3 %)	30 (100 %)	37.297	1	**.000*** **
	Present	23 (76.7 %)	0 (0 %)			
Diagnosis	F 30.2	6 (20 %)				
	F31.2	24 (80 %)				

(*p<0.05, **p<0.01, ***p<0.001) f = fischer's exact

The study recruited 30 male subjects with a diagnosis of either mania with psychotic symptoms or bipolar affective disorder current episode manic with psychotic symptoms, made according to the International Classification of Diseases-10 - DCR (WHO, 1993) and 30 male normal control. Chi-square test was applied and Fischer's exact test (where applicable) were applied to compare two groups of categorical variable. The socio-demographic variables of religion, residence, education, occupation, marital status, family income, past history, family history, treatment history and diagnosis are explained in Table 1. Out of 30 cases 6 (20%) had a diagnosis of mania with psychotic symptoms, and 24 (80%) had a diagnosis of bipolar affective disorder current

episode manic with psychotic symptoms, 20 (66.7%) were Hindus, and the rest 10 (33.3%) belonged to other religions, 26 (86.7%) resides in urban area, rest 4 (13.3 %) in rural area, 6 (20%) are educated till class 6, 23 (76.7%) are educated till class 12, 1 (3.3%) is graduate, 24 (80%) are employed, 14 (46.7%) is married, 26 (86.7%) have a family income below 12000, 24 (80%) have past psychiatric history, 11 (36.7%) have psychiatric illness in family, 23 (76.7%) took psychiatric medication in the past. Among 30 healthy controls 25 (83.3%) were Hindus, and the rest 5 (16.7 %) belonged to other religions, 2 (6.7%) are educated till class 12, 28 (93.3%) are graduate, 7 (23.3%) is married, 10 (33.3%) have a family income below 12000.

TABLE 2: COMPARISION OF AGE (CONTINUOUS VARIABLE) BETWEEN PATIENT GROUP OF BIPOLAR MANIA WITH ECT AND CONTROL GROUP [N=60]

Variable	Patient Group, N=30, Mean±SD	Control Group, N=30, Mean±SD	X^2/T	Df	P
Age (Years)	25.0 ± 5.8	26.5 ± 5.5	.977	58	.332

p=NS

In table 2 the mean age of patient group of bipolar mania with ECT and control group are compared. Here, t-test was applied to compare two groups of continuous variables. Mean age of cases are 25.0 ± 5.8, and control are 26.5 ± 5.5%. There is no significant difference between these two variables.

TABLE 3: COMPARISION OF BASELINE BLOOD PARAMETERS (CONTINUOUS VARIABLE) BETWEEN PATIENTS GRUOP OF BIPOLAR MANIA WITH ECT AND CONTROL GROUP [N=60]

	Patient Group, N=30, Mean±SD	Control Group, N=30, Mean±SD	t	df	p
FBS	86.433 ± 12.637	92.733 ± 39.921	.824	58	.413
CHOLESTEROL	123.667 ± 26.170	181.000 ± 40.268	6.539	58	**.000*** **
TRIGLYCERIDE	113.633 ± 48.957	132.033 ± 69.060	1.191	58	.239
HDL	40.066 ± 10.368	44.400 ± 8.743	1.750	58	.085
LDL	72.900 ± 21.849	105.566 ± 32.122	4.606	58	**.000*** **
VLDL	23.166 ± 10.780	26.500 ± 13.838	1.041	58	.302

(*p<0.05, **p<0.01, ***p<0.001)

In table 3, t-test was applied to compare two groups of continuous variable. Comparison has been made between blood parameters (fasting blood sugar, cholesterol, triglyceride, HDL, LDL, VLDL) of 30 cases which was taken at baseline just before 1st ECT and 30 normal healthy controls. There was significant difference between cases and controls in cholesterol (p=.000) and LDL (p=.000) with normal control have higher cholesterol and LDL.

TABLE 4: COMPARISION OF BLOOD PARAMETERS (CATEGORICAL VARIABLE) BETWEEN 1ST SAMPLE (TAKEN AT BASELINE, JUST BEFORE 1ST ECT), 2ND SAMPLE (20 MIN AFTER 1ST ECT) and 3RD SAMPLE (24 HOURS AFTER 1ST ECT)

	1ST SAMPLE (BASELINE)[1] MEAN ± SD	2ND SAMPLE (20 MIN AFTER ECT)[2] MEAN ± SD	3RD SAMPLE (24 HOURS AFTER ECT)[3] MEAN ± SD	df	F	p	POST HOC
FBS	86.433 ± 12.637	104.000 ± 15.611	87.800 ± 12.997	87	15.014	**.000*** **	2>1
CHOLESTEROL	123.667 ± 26.170	123.200 ± 26.966	123.166 ± 27.403	87	.003	.997	-
TRIGLYCERIDE	113.633 ± 48.957	107.500 ± 42.044	122.966 ± 59.124	87	.713	.493	-
HDL	40.066 ± 10.368	38.533 ± 9.565	37.366 ± 9.873	87	.557	.575	-
LDL	72.900 ± 21.849	74.700 ± 21.210	75.900 ± 21.238	87	.149	.862	-
VLDL	23.166 ± 10.780	21.433 ± 8.414	24.633 ± 11.781	87	.709	.495	-

(*p<0.05, **p<0.01, ***p<0.001)

In table 4 there is comparison between blood parameters (fasting blood sugar, cholesterol, triglyceride, HDL, LDL, VLDL) of 30 cases. Three samples were taken. 1st sample was taken at baseline, just before 1st ECT, 2nd sample was taken 20 min after 1st ECT and 3rd sample was taken 24 hours after 1st ECT. Here one way Anova and Post Hoc Bonferroni test was applied on continuous variable. There was significant increase in fasting blood sugar between 1st sample and 2nd sample, but no significant difference between 1st sample and 3rd sample. Regarding cholesterol, triglyceride, HDL, LDL and VLDL there was no significant difference between 1st sample, 2nd sample and 3rd sample.

TABLE 5: CORRELATION BETWEEN BASELINE BLOOD PARAMETERS WITH BASELINE YMRS, BPRS, MOAS and CGIS SCALES (CATEGORICAL VARIABLE) OF PATIENTS GROUP

	FBS		CHOLESTEROL		TRIGLYCERIDE		HDL		LDL		VLDL	
	r	p	r	p	r	p	r	p	r	p	r	P
YMRS1	.215	.254	.230	.221	.168	.376	.243	.196	.072	.706	.206	.274
BPRS1	.427	**.019***	.293	.115	.245	.192	.272	.147	.281	.133	.240	.202
MOAS1	.184	.330	.020	.918	.015	.936	.193	.308	.095	.618	.054	.777
CGIS1	.060	.753	.094	.620	.382	**.037***	.084	.660	.012	.951	.400	**.028***

(*p<0.05, **p<0.01, ***p<0.001)

In table 5 the correlation between baseline blood parameters and baseline scores of YMRS, BPRS, MOAS and CGIS of 30 cases is seen. Pearson's correlation was used for correlation of continuous variables. Significant correlation is seen between BPRS at baseline & baseline FBS (p = .019), between CGIS at baseline & baseline triglyceride (p= .037) & between CGIS at baseline & baseline VLDL (p= .028) of patient group.

TABLE 6: CORRELATION BETWEEN CHANGE IN FASTING BLOOD SUGAR BETWEEN 1ST SAMPLE (TAKEN AT BASELINE, JUST BEFORE 1ST ECT) and 2ND SAMPLE (20 MIN AFTER 1ST ECT) and NO OF ECT NEEDED FOR 50% REDUCTION IN YMRS and REDUCTION IN YMRS, BPRS, MOAS, CGIS and SCORE IN CGII AFTER 1ST ECT

	CHANGE IN FBS	
	R	p
NO OF ECT	.089	.639
CHANGE IN YMRS (1 and2)	.014	.943
CHANGE IN BPRS (1 and2)	.235	.211
CHANGE IN MOAS (1 and2)	.087	.649
CHANGE IN CGIS (1 and2)	.202	.283
CGII2	.179	.344

(*p<0.05, **p<0.01, ***p<0.001)

In table 6 change in fasting blood sugar between 1st sample (taken at baseline, just before 1st ECT) and 2nd sample (20 min after 1st ECT) is correlated with the number of ECT sessions needed for 50% reduction in YMRS scales and reduction in YMRS, BPRS, MOAS, CGIS (illness severity) scales after 1st ECT, from baseline and score in CGII (global improvement) after 1st ECT. The YMRS, BPRS, MOAS, CGIS (illness severity) scales were applied at baseline & after 1st ECT & the scores after 1st ECT were substracted from baseline scores, the CGII (global improvement) was scored after 1st ECT. Pearson's correlation was used for correlation of continuous variables. No significant correlation exists between these parameters.

IV. Discussion

The present study examined the post ECT change in blood sugar and lipid profile and correlated with psychopathology in patients of Bipolar disorder currently in mania or first episode mania. The study looked for the blood sugar and lipid profile changes seen immediately after ECT, 24 hours after ECT and compared it with the improvement in psychopathology.

DISCUSSION OF METHODOLOGY

The present study was conducted with a sample size of 30 male cases, with a diagnosis of either mania with psychotic symptoms (F 30.2) or bipolar affective disorder current episode manic with psychotic symptoms (F31.2), made according to the International Classification of Diseases-10 - DCR (WHO, 1993) and 30 male normal healthy control at a tertiary care hospital Central Institute of Psychiatry, Ranchi, catering primarily to a population from the eastern part of India. The earlier studies on effect of ECT were done on mostly on patients diagnosed as bipolar mania or depression & these studies usually took both male & female population (Rasmussen et al., 2006; Rasmussen and Ryan, 2005), while current study included only male patients. In one study 99 male & female patients was taken with diagnosis of depressive disorder, bipolar mood disorder or schizophrenia (Ghanizadeh et al., 2012). A few studies was done on diabetic patients to see the effect of ECT on blood sugar (Rasmussen et al., 2006; Netzel et al., 2002), while others were done on non-diabetic (Rasmussen and Ryan, 2005; Ghanizadeh et al., 2012), current study was done on non-diabetic patients. The study defined and studied a homogenous group of patients. Patients meeting the inclusion and exclusion criteria devised in present study was evaluated on sociodemographic and clinical data sheet. The study group was evaluated on Young Mania Rating Scale (YMRS), Clinical Global Improvement (CGI), Brief Psychiatric Rating Scale (BPRS) and Modified overt aggression scale (MOAS) at baseline and then on every alternate day after each

session of Modified ECT up to 50% improvement in YMRS scale. After 12 hours of fasting, 10ml of venous blood, using all aseptic precaution was collected from study group before first Modified ECT (at baseline), 20 minutes after first Modified ECT and 24hrs after the first modified ECT. This method was followed in earlier study where blood sample were collected from patients before and 20 minutes after ECT & evaluated for FBS & lipid profile to see the immediate effect of ECT (Ghanizadeh et al., 2012), while our study also included sustained effect of ECT, in addition to immediate effect on blood parameters. These blood samples were evaluated for fasting blood glucose and lipid profile on the same day at the institute's biochemistry laboratory. Earlier studies either used finger sticks to determine blood glucose (Rasmussen and Ryan, 2005) or taken blood sample (Ghanizadeh et al., 2012), & both methods were acceptable. The subjects included in the study group received Modified ECT treatment and 1st generation antipsychotic with or without mood stabilizer & excluded patients receiving 2nd generation mood stabilizer. Earlier studies more focused on confounding factors like exercise & diet rather than antipsychotic medication (Netzel et al., 2002). The number of Modified ECT patient receives was determined by the treating unit. The dose of medications was also determined by the treating unit and was recorded during each step of procedure. Subjects in control group was recruited from the hospital staff and community living in the vicinity of CIP. Written informed consent was taken after explaining the procedure in detail. Relevant socio-demographic and clinical data was collected from all the participants. Subjects in the control was screened with General Health Questionnaire (GHQ-12); only those with scored less than or equal to 3 was included. 10ml of venous blood using all aseptic precaution was collected from control group only once at 9:00 AM after 12 hours of fasting and was subjected for fasting blood sugar and lipid profile. Previous studies mostly didn't include any control groups.

DISCUSSION OF RESULTS

SAMPLE CHARACTERISTICS

Socio Demographic Characteristics and clinical variables

Our sample contains 30 male cases of first episode mania or bipolar mania and 30 normal controls. The mean age at onset for mania was 32.9 years. The mean age at first contact with a health professional for bipolar disorder was 31.2 years. Almost one-half of the male patients had onset of mania by age 25 years and 80%, by age 35 years (Kennedy et al., 2005). In a study of 100 patients two third were hospitalized before the age of 25, and at least 20% had already shown evidence of illness as adolescents. The early 20s was the peak period of onset (Kessler et al., 2005). Another study quoted ages 21 and 28 were derived from the+ analysis to define age-at-onset in bipolar patients (Kennedy et al., 2005). Study conducted on bipolar patients in 2002 relating panic disorder also showed the mean age of onset as 19.4±4.51 years (MacKinnon et al., 2002). The mean age of the patients in study group is 25.0 ± 5.8 years and normal control is 26.5 ± 5.5 years. Most of the patients being in between early and late adulthood. This represented the usual age of presentation of bipolar patients. Among 30 cases, 24 (80 %) of the patients in study group was employed, 14 (46.7%) are married and most of them belonging to the lower socio-economic status, 26 (86.7%) of them have family income <12000 rupees/ month. Most of the patients 20 (66.7%) had predominance of Hinduism which might be a reflection of the fact that Hinduism is the religion of the majority in India. In the control group is 25 (83.3 %) are Hindu, all 30 (100%) residing in urban areas, 28 (93.3 %) are graduate & all 30 (100%) employed. The sociodemographic variables of the patient group were compared with the normal control group using chi square test and Fischer's exact test (where applicable). There was significant difference between residence (p=.000), education(p=.000), occupation(p=.024) & family income (p=.000). The current study couldn't match the education status of patient & control, as per protocol, which is a limitation of the study.

Patients in study group are also assessed on various clinical parameters like past history, family history and treatment history of bipolar affective disorder. 24 (80%) out of 30 cases had past affective episodes and 23 (76.7%) of them received psychiatric treatment in the past, confirming the risk of recurrence in affective disorder. In previous study, it was found that there was significantly higher chance of recurrence in lifelong follow up (Angst et al., 2003). In the present study 11 (36.7%) out of 30 cases had positive family history, indicating a familial basis of the illness. Among BPAD patients there was increased prevalence of family history of affective illness. Previous studies indicated Familial aggregation of major affective disorders in bipolar pro-bands. Lifetime risks of first degree relatives and second degree relatives of affective disorder patients are 29.6% and 15.4% respectively (Strober, 1992).

The blood parameters of study group were done after 12 hours of fasting, at baseline, just before 1st ECT and control group was done once after 12 hours of fasting and both values compared. The mean total FBS level of study group in present study was 86.433 ± 12.637 mg/dl. The mean cholesterol level was 123.667 ± 26.170, TG level was 113.633 ± 48.957 mg/dl, and the mean HDL, LDL and VLDL levels were 40.066 ± 10.368 mg/dl, 72.900 ± 21.849 mg/dl and 23.166 ± 10.780 mg/dl respectively. On the other hand, the blood parameters of normal healthy control were the mean FBS level 92.733 ± 39.921 mg/dl, mean cholesterol level was 181.000 ± 40.268 mg/dl, TG level was 132.033 ± 69.060 mg/dl, and the mean HDL, LDL and VLDL levels

were 44.400 ± 8.743 mg/dl, 105.566 ± 32.122 mg/dl and 26.500 ± 13.838 mg/dl respectively. There was significant difference between study group and control group in cholesterol and LDL, with study group have statistically significantly lower cholesterol and LDL level. These findings are corroborative with previous study findings. Earlier study compared the lipid profiles in patients with bipolar mania (n=40) and normal controls (n=38) and found a significantly low levels of serum cholesterol and LDL that was independent of the body mass index (Sagud et al., 2007). Similarly, (Atmaca et al., 2002) found lower cholesterol levels amongst bipolar I patients and those with manic episodes, compared with controls. Thus, our findings add to the growing literature demonstrating a lower level of cholesterol and HDL in patients with bipolar disorder (Cassidy and Carroll, 2002; Fagiolini et al., 2005; Sagud et al., 2007; Fiedorowicz et al., 2008) compared to normal population.

Modified ECT and Blood Parameters

1st sample of blood taken from the study group, after 12 hours fasting, just before ECT, 2nd sample taken 20 minutes after ECT, to see the immediate effect and 3rd sample taken after 24 hours to see the sustained effect of ECT. The mean FBS of 1st, 2nd and 3rd sample were 86.433 ± 12.637, 104.000 ± 15.611 and 87.800 ± 12.997 respectively. The mean cholesterol of 1st, 2nd and 3rd sample were 123.667 ± 26.170, 123.200 ± 26.966 and 123.166 ± 27.403 respectively. The mean triglyceride of 1st, 2nd and 3rd sample were 113.633 ± 48.957, 107.500 ± 42.044 and 122.966 ± 59.124 respectively. The mean HDL of 1st, 2nd and 3rd sample were 40.066 ± 10.368, 38.533 ± 9.565 and 37.366 ± 9.873 respectively. The mean LDL of 1st, 2nd and 3rd sample were 72.900 ± 21.849, 74.700 ± 21.210 and 75.900 ± 21.238 respectively. The mean VLDL of 1st, 2nd and 3rd sample were 23.166 ± 10.780, 21.433 ± 8.414, 24.633 ± 11.781 respectively. There was significant increase in blood sugar in the 2nd sample as compared to 1st sample, but no significant difference between 1st and 3rd sample. In other words, there was immediate rise of blood sugar 20 minutes after ECT, but the rise was not sustained till 24 hours. Lipid profile parameters shown no significant immediate or sustained change with ECT. These findings corroborates with earlier study results. One study was done on 99 subjects irrespective of their psychiatric diagnosis, which showed that the ECT increases blood sugar and cholesterol level immediately after ECT, but ECT had no effect on triglyceride, HDL, LDL and VLDL. The increase of blood sugar after electroconvulsive therapy is mainly related to its effect on cortisol and norepinephrine. Electroconvulsive therapy acts as a stress and increases cortisol and norepinephrine, which increases the blood sugar immediately (Ghanizadeh et al., 2012). Another study also showed that blood glucose level was increased 20 minutes after electroconvulsive therapy in patients with severe depression and type II diabetes mellitus (Rasmussen et al., 2006). It is also studied that electroconvulsive therapy decrease the response to insulin, which might be one of the explanation of increase in blood sugar in diabetic patients (Williams et al., 1992). Dangerous hyperglycemia is also reported after electroconvulsive therapy (Reddy and Nobler, 1996). In a few studies the results were contrary. It was observed in one study, that in non-diabetic patients the blood glucose doesn't rise 20 minutes after electroconvulsive therapy (Rasmussen and Ryan, 2005). Again, another study showed that the electroconvulsive therapy have no significant effect on blood sugar in patients of insulin dependent type II diabetes mellitus (Netzel et al., 2002). There are very few studies on the effect of electroconvulsive therapy on lipid profile. In one study, it is seen that electroconvulsive therapy increases the total cholesterol level. But exact mechanism for this rise is not known. On the other hand, there is no evidence to support effect on LDL, HDL and triglyceride level, pre and post ECT of these parameters remains same (Kurt et al., 2007). In these studies, the sustained effect of ECT is not studied, while current study showed that there is no sustained effect of ECT on blood parameters after 24 hours.

Change in Blood Sugar and Its Correlation with Symptom Improvement

The baseline values of FBS, cholesterol, triglyceride, HDL, LDL, VLDL are correlated with baseline values of Young Mania Rating Scale, Brief Psychiatric Rating Scale, Modified overt aggression scale and Clinical Global Improvement (illness severity). Significant correlation is seen between BPRS at baseline & baseline FBS (p = .019), between CGIS at baseline & baseline triglyceride (p= .037) & between CGIS at baseline & baseline VLDL (p= .028) of patient group. But there is not any evidence in earlier studies to support this findings.

Earlier studies though observed increase in blood sugar after ECT, didn't studied the aspect of correlation of increase in blood sugar with symptom improvement, whether the symptom improvement was faster or more robust with ECT, in patients, in whom blood sugar hike is more pronounced. In other word, whether blood sugar increase with ECT can predict response to ECT or not (Ghanizadeh et al., 2012). Current study correlated immediate increase in blood sugar and correlated with two different parameters, one is number of ECT needed for 50% improvement in YMRS scores and another is decrease in score of YMRS, BPRS, MOAS and CGI (illness severity) and score in CGI (improvement) after 1st ECT. The YMRS, BPRS, MOAS,

CGIS (illness severity) scales were applied at baseline & after 1st ECT & the scores after 1st ECT were substracted from baseline scores, the CGII (global improvement) was scored after 1st ECT. Pearson's correlation was used for correlation of continuous variables. Our study found no significant correlation between blood sugar increase & symptom improvement. So according to our study blood sugar increase with ECT, can't predict response to ECT.

V. Conclusion

The current study demonstrates the presence of statistically significantly lower cholesterol and LDL level in study group. Also, this study explored that ECT increases blood sugar immediately, but the rise is not sustained and this rise in blood sugar have no correlation with symptom improvement in bipolar mania. This is a novel finding because the earlier studies didn't measure whether the rise is sustained and it have any correlation with symptom improvement or not.

References

[1]. Angst, J., Gamma, A., Sellaro, R., Lavori, P., & Zhang, H. (2003). Recurrence of bipolar disorders and major depression. *European archives of psychiatry and clinical neuroscience*, *253*(5), 236-240.

[2]. Atmaca, M., Kuloglu, M., Tezcan, E., Ustundag, B., & Bayik, Y. (2003). Serum leptin and cholesterol levels in patients with bipolar disorder. *Neuropsychobiology*, *46*(4), 176-179.

[3]. Cassidy, F., & Carroll, B. J. (2002). Hypocholesterolemia during mixed manic episodes. European archives of psychiatry and clinical neuroscience, 252(3), 110-114.

[4]. Fagiolini, A., Frank, E., Scott, J. A., Turkin, S., & Kupfer, D. J. (2005). Metabolic syndrome in bipolar disorder: findings from the Bipolar Disorder Center for Pennsylvanians. Bipolar disorders, 7(5), 424-430.

[5]. Fiedorowicz, J. G., Leon, A. C., Keller, M. B., Solomon, D. A., Rice, J. P., & Coryell, W. H. (2009). Do risk factors for suicidal behavior differ by affective disorder polarity?. Psychological medicine, 39(05), 763-771

[6]. Fink, M. (2000). Electroshock revisited. *American Scientist*, *88*(2), 162-179.

[7]. Ghanizadeh, A., Issaee, M., Sigaroody, M. O., & Kaviani, K. (2012). The effect of electroconvulsive therapy on blood glucose, creatinine levels, and lipid profile and its association with the type of psychiatric disorders. *Neurochemistry international*, *61*(7), 1007-1010.

[8]. Goldberg, D. (2000). Plato versus Aristotle: categorical and dimensional models for common mental disorders. *Comprehensive psychiatry*, *41*(2), 8-13.

[9]. Hedlund, J. (1980). *The brief psychiatric rating scale (BPRS): A comprehensive review*.

[10]. International Classification of Diseases-10 - DCR (WHO, 1993)

[11]. Kennedy, N., Boydell, J., Kalidindi, S., Fearon, P., Jones, P. B., van Os, J., & Murray, R. M. (2005). Gender differences in incidence and age at onset of mania and bipolar disorder over a 35-year period in Camberwell, England. *American Journal of Psychiatry*, *162*(2), 257-262.

[12]. Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). " Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey replication": Erratum.

[13]. Kurt, E., Guler, O., Serteser, M., Cansel, N., Ozbulut, O., Altınbaş, K., ... & Gecici, O. (2007). The effects of electroconvulsive therapy on ghrelin, leptin and cholesterol levels in patients with mood disorders. Neuroscience letters, 426(1), 49-53.

[14]. MacKinnon, D. F., Zandi, P. P., Cooper, J., Potash, J. B., Simpson, S. G., Gershon, E., ... & DePaulo, J. R. (2002). Comorbid bipolar disorder and panic disorder in families with a high prevalence of bipolar disorder. *American Journal of Psychiatry*, *159*(1), 30-35.

[15]. Mukherjee, S., & Debsikdar, V. (1992). Unmodified Electroconvulsive Therapy of Acute Mania: A Retrospective Naturalistic Study.

[16]. Mukherjee, S., Sackeim, H. A., Schnur, D. B., Breier, A., & Talbott, J. A. (1995). Electroconvulsive Therapy of Acute Manic Episodes: A Review of 50 Years' Experience. *Year Book of Psychiatry & Applied Mental Health*, *1995*(10), 469-470.

[17]. Netzel, P. J., Mueller, P. S., Rummans, T. A., Rasmussen, K. G., Pankratz, V. S., & Lohse, C. M. (2002). Safety, efficacy, and effects on glycemic control of electroconvulsive therapy in insulin-requiring type 2 diabetic patients. *The journal of ECT*, *18*(1), 16-21.

[18]. Rasmussen, K. G., & Ryan, D. A. (2005). The effect of electroconvulsive therapy treatments on blood sugar in nondiabetic patients. *The journal of ECT*, *21*(4), 232-234.

[19]. Rasmussen, K. G., Ryan, D. A., & Mueller, P. S. (2006). Blood glucose before and after ECT treatments in Type 2 diabetic patients. *The journal of ECT*, *22*(2), 124-126.

[20]. Ratey, J. J., & Gutheil, C. M. (1991). The measurement of aggressive behavior: Reflections on the use of the Overt Aggression Scale and the modified Overt Aggression Scale. *The Journal of neuropsychiatry and clinical neurosciences*.

[21]. Reddy, S., & Nobler, M. S. (1996). Dangerous hyperglycemia associated with electroconvulsive therapy. The Journal of ECT, 12(2), 99-103.

[22]. Sagud M, Mihaljevic-Peles A, Pivac N, Jakovljevic M, Muck-Seler D. Platelet serotonin and serum lipids in psychotic mania. Journal of affective disorders. 2007 Jan 31;97(1):247-51.

[23]. Sikdar, S., Kulhara, P., Avasthi, A., & Singh, H. (1994). Combined chlorpromazine and electroconvulsive therapy in mania. *The British Journal of Psychiatry*, *164*(6), 806-810.

[24]. Spearing, M. K., Post, R. M., Leverich, G. S., Brandt, D., & Nolen, W. (1997). Modification of the Clinical Global Impressions (CGI) Scale for use in bipolar illness (BP): the CGI-BP. *Psychiatry research*, *73*(3), 159-171.

[25]. Strober, M. (1992). Relevance of early age-of-onset in genetic studies of bipolar affective disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *31*(4), 606-610.

[26]. Thomas, J., & Reddy, B. (1982). The treatment of mania: a retrospective evaluation of the effects of ECT, chlorpromazine, and lithium. *Journal of affective disorders*, *4*(2), 85-92.

[27]. Williams, K., Smith, J., Glue, P., & Nutt, D. (1992). The effects of electroconvulsive therapy on plasma insulin and glucose in depression. The British Journal of Psychiatry, 161(1), 94-98.

[28]. Young, R. C., Biggs, J. T., Ziegler, V. E., & Meyer, D. A. (1978). A rating scale for mania: reliability, validity and sensitivity. *The British Journal of Psychiatry*, *133*(5), 429-435.