Observational Study of Effects of Saroglitazar on Glycaemic and Lipid Parameters on Indian Patients with Type 2 Diabetes

Sanjay Chatterjee¹, Anirban Majumder² & Subir Ray³

¹Consultant Diabetologist, Apollo Gleneagles Hospital, 58 Canal Circular Road, Kolkata 700054, India, ²Associate Professor, Department of Medicine, Endocrinology Unit, KPC Medical College, Kolkata 700032, India, ³Consultant Endocrinologist, Apollo Gleneagles Hospital, 58 Canal Circular Road, Kolkata 700054, India.

Cardiovascular risk reduction is an important issue in the management of patients with Type 2 diabetes mellitus. Peroxisome proliferator–activated receptor (PPAR) agonists favourably influence glycaemic and lipid parameters in patients with Type 2 diabetes and a dual PPAR agonist is expected to have favourable effect on both parameters. In this study we have analyzed the effect of Saroglitazar, a novel dual PPAR alpha & gamma agonist, on glycaemic and lipid parameters in Indian patients with Type 2 diabetes. After a mean follow-up period of 14 weeks in 34 patients, treatment with Saroglitazar, in a dose of 4 mg daily, resulted in significant improvement in both glycaemic and lipid parameters. There were significant mean reductions of fasting plasma glucose (36.71 mg/dl; p = 0.0007), post-prandial plasma glucose (66.29 mg/dl; p = 0.0005), glycosylated haemoglobin (1.13%; p < 0.0001), total cholesterol (48.16 mg/dl; p < 0.0001), low-density lipoprotein cholesterol (24.04 mg/dl; p = 0.0048), triglyceride (192.78 mg/dl; p = 0.0001), non-high density lipoprotein cholesterol (48.72 mg/dl; p < 0.0001) and the ratio of triglyceride and high density lipoprotein cholesterol (5.30; p = 0.0006). There was no significant change in body weight, blood pressure, high-density lipoprotein cholesterol and serum creatinine.

Insulin resistance is an integral part of Type 2 diabetes mellitus. The components of insulin resistance are obesity, dysglycaemia, dyslipidaemia and hypertension – all of which have adverse effects on cardiovascular system. Since cardiovascular death is the most important cause of mortality for patients with Type 2 diabetes, cardiovascular risk reduction is of paramount importance while treating patients with Type 2 diabetes. At present, the available means of cardiovascular risk reduction in diabetic patients are lifestyle changes (exercise, diet, cessation of tobacco), control of hypertension, glycaemic control and management of lipid abnormalities. Peroxisome proliferator–activated receptors (PPARs) are transcription factors belonging to the superfamily of nuclear receptors. Three isoforms, alpha, gamma & delta have been described. They act on DNA response elements as heterodimers with the nuclear retinoic acid receptor. Their natural activating ligands are fatty acids and lipid-derived substrates.

PPAR-alpha is present in liver, heart, and, to a lesser extent, in skeletal muscle. When activated, it promotes fatty acid oxidation, ketone body synthesis, and glucose sparing. Fibrates, which are used as hypolipidaemic drugs, are ligands of PPAR-alpha. PPAR-gamma is expressed in adipose tissue, lower intestine, and cells involved in immunity. Activation of PPAR-gamma induces the differentiation of preadipocytes into adipocytes and stimulates triglyceride storage. Thiazolidinediones (TZDs) are activators of PPAR-gamma. Their action on muscle insulin sensitivity may be secondary to the lowering of circulating lipids and to the secretion of insulin-sensitizing hormones such as adiponectin, and promote glucose utilization. PPAR-delta is ubiquitous and could also favor fatty acid oxidation in tissues where PPAR-alpha is absent, and possibly involved in immunomodulation. The PPARs are thus major regulators of lipid and glucose metabolism.

The fibrates are PPAR-alpha agonists and reduce triglyceride and increase HDL levels in blood. In Bezafibrate Infarction Prevention (BIP) trial and Veterans Affairs High-Density Lipoprotein Cholesterol Intervention (VA-HIT) trial, use of fibrates was shown to reduce cardiovascular risk.
The thiazolidinediones (TZDs) are PPAR-gamma agonists and improve glycaemia in patients with Type 2 diabetes. The TZDs improve glycaemia but may cause weight gain and fluid retention. Fibrates may increase serum creatinine level, liver enzymes and when used with statins, may increase myositis. Drugs which are dual agonists of both PPAR-alpha and PPAR-gamma are being developed with the hope of improving glycaemic and lipid parameters and thereby reducing cardiovascular risk in Type 2 diabetes patients. This group of drugs has been named “glitazar”.

Saroglitazar, [(S)-a-ethoxy-4-[2-[2-methyl-5-(4-methylthio) phenyl]-1H-pyrorol-1-yl]-ethoxy]-benzeneproanoic acid magnesium salt, is the first glitazar to receive marketing approval and has been granted marketing permission in India in June 2013 in the name Lipaglyn®. At present it is available as 4 mg tablets. In clinical trials, saroglitazar has reduced triglyceride levels with modest reductions in HbA1c.

As results obtained in randomized clinical trials may vary from that obtained in clinical practice, we wanted to see the effects of saroglitazar on lipids and also on glycaemic parameters on our patients with Type 2 diabetes mellitus.

Methods
Saroglitazar was prescribed in a dose of 4 mg daily, in accordance with approved guidelines, to patients with Type 2 diabetes and having hypertriglyceridaemia (serum triglyceride level > 150 mg/dL). Patients received treatment as par standard of care and no experiment was done on any patient. Only data of patients with pre- and post-treatment values are direct, not calculated from Friedewald equation. Only there was sufficient data is direct, not calculated from Friedewald equation. Only there was sufficient data and it was measured by HPLC (BioRad D-10, Bio-RAD, Hercules, CA, USA). The LDL was measured by HPLC (BioRad D-10, Bio-RAD, Hercules, CA, USA). The LDL was measured by HPLC (Hercules, CA, USA). The LDL was measured by HPLC (Hercules, CA, USA). The LDL was measured by HPLC (Hercules, CA, USA). The LDL was measured by HPLC (Hercules, CA, USA). The LDL was measured by HPLC.

Blood glucose was measured by Hexokinase method. Creatinine (Jaffe Kinetic), ALT (IFCC, without P5P), Cholesterol (Cholesterol oxidase – CHOD/PAP), HDL (Direct Immunoinhibition), Triglyceride (Glycerol-3 phosphate oxidase) and HbA1c was measured by HPLC (BioRad D-10, Bio-RAD, Hercules, CA, USA). The LDL values are direct, not calculated from Friedewald equation. Only there was sufficient data of 34 patients that was fit for analysis. The mean follow-up duration was 14 weeks.

Results
Out of total 34 patients included in the study, 23 were male. The age of the patients was between 28 and 72 years and mean age was 52 years. All patients had Type 2 diabetes mellitus and dyslipidaemia. Other significant co-morbidities are given in Table 1. Baseline parameters of patients are shown in Table 2.

Change in weight, blood pressure, creatinine and ALT (Table 3): There has been a slight weight gain, mean 0.71 Kg in the 14 weeks’ follow-up period; however, this change is not statistically significant (p = 0.07). All patients received antidiabetic medication, including insulin, sulfonylurea and one received pioglitazone – all of which are known to cause weight gain. There was no significant change in systolic or, diastolic blood pressure and serum creatinine level following therapy with saroglitazar. However, there was a small but significant reduction of serum ALT (mean reduction 9.69 U/L, p = 0.03).

Effect on blood glucose (Table 4): There were significant reductions in both fasting and post-prandial plasma glucose levels. There was also significant reduction in HbA1c level. However, it should be mentioned that antidiabetic medication was modified in 19 patients because of high blood glucose level at baseline. Even in patients whose antidiabetic medication was not changed (n = 13), there was a modest and significant drop in HbA1c (Table 5).

Effects on serum lipids (Table 4): There were significant reductions in total cholesterol, LDL cholesterol and triglyceride (Table 4). In spite of the robust and significant reduction in total cholesterol, HDL-cholesterol level remained unaltered. Twenty five patients were receiving statins (atorvastatin 10 mg or, rosuvastatin 10 mg daily) at

### Table 1 | Comorbidities

| Comorbidities        | Number |
|----------------------|--------|
| Overweight/Obesity   | 12     |
| Hypertension         | 20     |
| Hypothyroidism       | 1      |
| Microalbuminuria     | 4      |
| Fatty Liver (by USG) | 7      |

| Comorbidities      | %  |
|--------------------|----|
| Overweight/Obesity | 35.29 |
| Hypertension       | 58.8  |
| Hypothyroidism     | 2.94   |
| Microalbuminuria   | 11.7    |
| Fatty Liver (by USG) | 20.5 |

### Table 2 | Baseline Characteristics

| Demographic Profile | Male (number) | 23 |
|---------------------|---------------|----|
| Female (number)     | 11            | 52.33 [28-72] |
| Age Mean [Range] (yrs) | 52.33 [28-72] |
| Weight Mean = SD (Kgs) | 69.14 ± 9.56 |

| Laboratory data     | 160.53 ± 53.71 |
|---------------------|-----------------|
| FPG Mean = SD (mg/dL) | 243.68 ± 114.59 |
| PPG Mean = SD (mg/dL) | 8.34 ± 1.58   |
| HbA1c Mean = SD (%)  | 195.91 ± 56.97 |
| Total Cholesterol Mean = SD (mg/dL) | 346.78 ± 246.01 |
| Triglycerides Mean = SD (mg/dL) | 38.88 ± 9.79   |
| HDL Mean = SD (mg/dL) | 108.34 ± 46.94 |
| LDL Mean = SD (mg/dL) | 157.34 ± 53.44 |
| Non HDL Mean = SD (mg/dL) | 9.60 ± 7.84   |
| TG/HDLC ratio Mean = SD | 52.83 ± 31.96 |
| ALT Mean = SD (IU/L) | 0.95 ± 0.21   |

Abbreviations: FPG, fasting plasma glucose; PPG, post prandial glucose; HbA1c, glycylsated haemoglobin; ALT, Alanine aminotransferase; HDL, high-density lipoprotein; LDL, low-density; non HDL, non high density lipoprotein; TG, triglycerides; S-Cr, Serum Creatinine
baseline. The addition of Saroglitazar favourably altered the lipid profile of the patients, irrespective of concomitant statin therapy. There was significant reduction in non-HDLc level, thereby causing a residual risk-reduction. Five patients had a baseline triglyceride level of less than 200 mg/dl. In those five patients also there were improvement in lipid and glycaemic parameters (Table 6). Another important finding is the robust reduction in triglyceride/HDLc ratio, and this may have a favourable effect on LDL particle size. The TG/HDLc ratio is a better index of LDL particle size than the level of triglyceride. A reduction of both triglyceride and TG/HDLc ratio shift small dense LDL particles to more buoyant and larger LDL particles which are less atherogenic.

Side-effects: Two patients complained of minor hypoglycaemia – both of them were taking sulfonylurea. One patient complained of general weakness (asthenia), one patient complained of loss of appetite. Saroglitazar was discontinued in three patients at last visit – one patient had high serum ALT and AST at baseline and also at last visit; in two patients, there was no reduction in serum triglyceride level. No serious adverse event was reported by any patient receiving saroglitazar.

Discussion

The recently published American College of Cardiology (ACC)/American Heart Association (AHA) guideline on lipid management focussed on cardiovascular risk assessment and use of statins in patients with different categories of cardiovascular risk. The guideline also suggested avoiding medications or, supplements that may lower the cholesterol number but have no data to decrease cardiovascular risk.

Whereas earlier studies with fibrates, like BIP or, VA-HIT showed nearly one-third risk reduction in cardiovascular events, more recent trials like Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study or, Action to Control Cardiovascular Risk in Diabetes (ACCORD)-Lipid arm failed to show such benefit.

The FIELD study was done with 9795 patients who were randomized to fenofibrate or, placebo. After 5 years, there was a non-significant increase (110 vs 93) in cardiovascular deaths in fenofibrate group. However, there was a significant reduction non-fatal M.I. and also of coronary revascularization in fenofibrate group. It is also to be noted that FIELD study included patients with triglyceride level of 1 mmol/L (89 mg/dl) or higher and the benefit of triglyceride reduction was evident in patients whose initial levels were high.

Result of the ACCORD-lipid arm showed no cumulative benefit of adding fenofibrate to simvastatin. However, when subgroup analysis was done, significant cardiovascular benefit was noted in patients who had a high triglyceride level (>204 mg/dl) and the benefit was found only in male patients. Therefore, addition of PPAR-alpha agonist gemfibrozil (VA-HIT study), bezafibrate (BIP study) and fenofibrate (FIELD and ACCORD-Lipid) did show cardiovascular benefit. The benefit is probably mediated through reduction in triglyceride, particularly when its level is high, rather than a direct vascular or, pleiotrophic effect, like the statins.

There is unequivocal evidence of cardiovascular benefit of lowering LDL in several clinical trials with statins.

However, LDL morphology changes with increase in serum triglyceride level. A study showed that when triglyceride level reaches 250 mg/dl, 85% LDL particles become small and dense – these small, dense LDL particles are highly Atherogenic.

A meta-analysis of 40 randomized controlled trials showed that the proportional difference in triglyceride levels was predictive of cardiovascular events in all trials (P = 0.005 for the slope of the regression line). However this predictive value is present in primary prevention trials (P = 0.010; N = 11), but not in secondary prevention trials (P = 0.114; N = 25). The LDLc levels were predictive of cardiovascular events in both primary (P = 0.002; N = 11) and secondary (P < 0.001; N = 25) populations.

In 2012, the American Association of Clinical Endocrinologists (AACE) recommended to calculate non–HDLc in patients with moderately elevated TG (200–500 mg/dL) with diabetes mellitus and/or established CAD. In patients with insulin resistance, AACE recommended evaluating non-HDLc to gain useful information regarding the patient’s total atherogenic lipoprotein burden. The guidelines also opined that in any circumstance when triglycerides are 200–499 mg/dl, a non–HDLc calculation would provide better risk assessment than LDLc alone.

In 2013, the AACE further re-iterated that Non-HDLc goal should be achieved with triglyceride lowering therapy after achievement of desirable LDLc level.

A meta-analysis of 25 trials (n = 131,134) on lipid lowering therapy suggested that Non- HDLc modestly outperforms Apo-B for prediction of CHD.

Meta-analysis of 62,154 statin-treated patients in 8 trials published between 1994 and 2008 showed that 1 SD increase in non-HDLc, raises risk of CV events by 16%, whereas 1 SD increase in LDLc, increases risk of CV events by 13% (p = 0.002 Vs. LDLc). The

Table 3 | Change in weight, ALT, creatinine and blood pressure

| Parameter         | Baseline Mean ± SD | Follow up Mean ± SD | Mean change ± SD | P value |
|-------------------|--------------------|---------------------|------------------|---------|
| Weight (Kgs)      | 69.14 ± 9.56       | 69.85 ± 10.52       | +0.71 ± 0.78     | 0.07    |
| ALT Mean (IU/L)   | 52.83 ± 31.96      | 43.17 ± 27.84       | −9.69 ± 9.05     | 0.03    |
| S. Cr (mg/dl)     | 0.95 ± 0.21        | 1.04 ± 0.24         | +0.09 ± 0.10     | 0.06    |
| SBP (mmHg)        | 131.70 ± 14.81     | 127.77 ± 10.71      | −4.35 ± 4.20     | 0.06    |
| DBP (mmHg)        | 80.67 ± 5.94       | 79.00 ± 4.87        | −1.39 ± 0.54     | 0.2     |

Table 4 | Laboratory values: Change from baseline

| Lab parameters    | Baseline Mean ± SD | Follow up Mean ± SD | Mean change ± SD | P value |
|-------------------|--------------------|---------------------|------------------|---------|
| Triglycerides (mg/dl) | 346.78 ± 246.01  | 154.00 ± 127.73  | −192.78 ± 91.06 | 0.0001  |
| Non HDLc (mg/dl)   | 157.34 ± 53.44    | 108.63 ± 34.47    | −48.72 ± 17.09  | <0.0001 |
| LDLc (mg/dl)       | 108.34 ± 46.94    | 84.31 ± 23.26     | −24.04 ± 16.14  | 0.0048  |
| Total Cholesterol (mg/dl) | 195.91 ± 56.97 | 147.75 ± 36.08 | −48.16 ± 17.32 | <0.0001 |
| HDLc (mg/dl)       | 38.88 ± 9.79      | 39.34 ± 11.37     | +0.47 ± 3.45    | 0.7836  |
| TG/HDL ratio       | 9.60 ± 7.84       | 4.30 ± 4.12       | −5.30 ± 2.82    | 0.0006  |
| FPG (mg/dl)        | 160.53 ± 53.71    | 123.82 ± 54.91    | −36.71 ± 20.06  | 0.0007  |
| PPG (mg/dl)        | 243.68 ± 114.59   | 177.39 ± 60.87    | −66.29 ± 34.71  | 0.0005  |
| HbA1c (%)          | 8.34 ± 1.58       | 7.21 ± 1.33       | −1.13 ± 0.43    | <0.0001 |
glitazar appeared to be an effective and safe therapeutic option for arm and no persistent change in laboratory parameters. Saroglitazar treatment reduced (P<0.001) plasma triglyceride from baseline by 45% (absolute change ± SD: −115.4 ± 68.11 mg/dL), respectively, as compared to pioglitazone −15.5% (absolute change ± SD: −33.3 ± 162.41 mg/dL) at week 24. Saroglitazar 4 mg treatment also demonstrated marked decrease in low-density lipoprotein (5%), very-low-density lipoprotein (45.5%), total cholesterol (7.7%), and apolipoprotein B (10.9%). Saroglitazar treatment was generally safe and well tolerated. No serious adverse events were reported in saroglitazar treatment arm and no persistent change in laboratory parameters. Saroglitazar appeared to be an effective and safe therapeutic option for improving hypertriglyceridemia in patients with type 2 diabetes mellitus.

In our study, we have found more robust reduction in triglyceride and HbA1c. The probable reason was the baseline triglyceride was higher in our study and also possibly due to improvement in glycemia that might have helped in reduction of triglyceride level.

Several dual PPAR-alpha/gamma agonists have been developed for therapeutic use. The development of tesaglitazar, the first glitazar developed, was withdrawn for renal safety issues. Another dual PPAR-agonist, muraglitazar, was discontinued due to higher risk of cardiovascular events. Moreover, in clinical studies, both muraglitazar and tesaglitazar increased weight gain and edema like pioglitazone.

Another compound in this class, aleglitazar, caused less weight gain and showed better lipid effects and similar glycemic control, compared to pioglitazone. But it failed to show cardiovascular benefit in randomized controlled trial. Effect of Aleglitazar on Cardiovascular Outcomes After Acute Coronary Syndrome in Patients With Type 2 Diabetes Mellitus (AleCardio) trial was prematurely stopped due to increase in heart failure (3.4% for aleglitazar vs 2.8% for placebo, P = 0.14), gastrointestinal haemorrhages (2.4% for aleglitazar vs 1.7% for placebo, P = 0.03), and renal dysfunction (7.4% for aleglitazar vs 2.7% for placebo, P < 0.001). Saroglitazar, the only glitazar approved for clinical use, has shown good efficacy and safety in short-term use. In our study, we have observed similar benefit on lipid glycemic parameters as found in clinical trials. However, there was slight, but statistically insignificant, increase serum creatinine and body weight. Future studies will throw more light on these aspects. As per regulatory requirement, a Phase IV (post-marketing surveillance) study, named PRESS X, (Trial registration no. CTRI/2013/06/003754) is in progress. The study will compare the safety and efficacy of fenofibrate 160 mg daily with saroglitazar 2 mg or 4 mg daily for a period of 24 weeks and the sample size will be 1010. We also look forward to a cardiovascular outcome study of saroglitazar to see correlation of triglyceride and non-HDLc on cardiovascular outcome.

**Conclusion**

Dyslipidaemia in diabetes has some unique features and may require specific consideration. This is the first report of clinical use of a dual PPAR alpha/gamma agonist on Type 2 diabetic patients with dyslipidemia. The use of dual PPAR alpha/gamma agonist, saroglitazar, for a period of 14 weeks, was associated with significant improvement in both glycaemic and lipid parameters among Indian patients with Type 2 diabetes. Overall saroglitazar was well tolerated and there was no serious adverse event reported.

**Limitations of this study**

This is the first report of clinical use of saroglitazar, for a mean 14 weeks' duration with a small number of patients. We could not assess adherence to therapy or, use of concomitant medications in our patients. Therefore, more studies from India with larger sample size and longer duration will be necessary to validate our findings.

---

1. Solano, M. P. & Goldberg, R. B. Lipid Management in Type 2 Diabetes. *Clinical Diabetes* 24, 27–32 (2006).
2. Garber, A. J. et al. Non HDL-C targets are 30 mg/dl higher than established LDL-C risk levels AACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM 2013. Endocer Pract 19, 1–48 (2013).

3. Nicholls, S. J. & Uno, K. Peroxisome proliferator-activated receptor (PPAR a/c) agonists as apotential target to reduce cardiovascular risk in diabetes. Diabetes Vasc Dis Res 9, 89–94 (2012).

4. The BIP Study Group. Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease: the Bezafibrate Infarction Prevention (BIP) study. Circulation 102, 21–7 (2000).

5. Rubins, H. B. et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. N Engl J Med 341, 410–419 (1999).

6. Jani, R. H. et al. A multicenter, prospective, randomized, double-blind study to evaluate the safety and efficacy of Saroglitazar 2 and 4 mg compared with placebo in type 2 diabetes mellitus patients having hypertriglyceridemia not controlled with atorvastatin therapy (PRESS VI). Diabetes Technol Ther 16, 63–71 (2014).

7. Boizel, R. et al. Ratio of triglycerides to HDL cholesterol is an indicator of LDL particle size in patients with type 2 diabetes and normal HDL cholesterol levels. Diabetes Care 23, 1679–85 (2000).

8. Stone, N. J. et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 24, 129, S1–45 (2014).

9. Keech, A. et al. (FIELD study investigators). Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet 366, 1849–1861 (2005).

10. The ACCORD Study Group. "Effects of combination lipid therapy in type 2 diabetes mellitus.” N Engl J Med 362, 1563–1574 (2010).

11. Elley, C. R. Statins reduce mortality and major vascular events in patients with no history of CV disease. ACP Journal Club Review. Ann Intern Med 159, J2. (2013).

12. Austin, M. A., King, M. C., Vranizan, K. M. & Krauss, R. M. Atherogenic lipoprotein phenotype. A proposed genetic marker for coronary heart disease risk. Circulation 82, 495–506 (1990).

13. Stauffer, M. E., Weisenfluh, L. & Morrison, A. Association between triglycerides and cardiovascular events in primary populations: a meta-regression analysis and synthesis of evidence. Vasc Health Risk Manag 9, 671–680 (2013).

14. Jellinger, P. S. et al. (The AACE Task Force for Management of Dyslipidemia and Prevention of Atherosclerosis). AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS' GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OFATHEROSCLEROSIS. Endocer Pract 18, 1–78 (2012).

15. Garber, A. J. et al. Non HDL-C targets are 30 mg/dl higher than established LDL-C risk levels AACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM 2013. Endocer Pract 19, 1–48 (2013).

16. Robinson, J. G., Wang, S. & Jacobson, T. A. Meta-analysis of comparison of effectiveness of lowering apolipoprotein B versus low-density lipoprotein cholesterol and nonhigh-density lipoprotein cholesterol for cardiovascular risk reduction in randomized trial. Am J Cardiol 110, 1468–1476 (2012).

17. Boekholdt, S. M. et al. Association of LDL Cholesterol, Non-HDL Cholesterol, and Apolipoprotein B Levels With Risk of Cardiovascular Events Among Patients Treated With Statins - A Meta-analysis. J Am Med Assoc 307, 1302–1309 (2012).

18. Statement by the American Diabetes Association Regarding the American College of Cardiology/American Heart Association Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. (URL: http://www.diabetes.org/newsroom/press-releases/2013/statement-cholesterol-guidelines.html.) Published 2013. Date accessed 10/08/2014.

19. Nordestgaard, B. G. & Varbo, A. Triglycerides and cardiovascular disease. Lancet 384, 626–635 (2014).

20. Pai, V. et al. Multicenter, Prospective, Randomized, Double-blind Study to Evaluate the Safety and Efficacy of Saroglitazar 2 and 4 mg Compared to Pioglitazone 45 mg in Diabetic Dyslipidemia (PRESS V). J Diabetes Sci Technol 8, 132–141 (2014). [Epub ahead of print].

21. Dietz, M. et al. Comparative Molecular Profiling of the PPARa/γ Activator Aleglitazar: PPAR Selectivity, Activity and Interaction with Cofactors. Chem MedChem 7, 1101–1111 (2012).

22. Lincoff, A. M. et al. (2014) Effect of aleglitazar on cardiovascular outcomes after acute coronary syndrome in patients with type 2 diabetes mellitus: the AleCardio randomized clinical trial J Am Med Assoc 311, 515–25 (2014).

23. A phase IV clinical study to evaluate the safety and efficacy of Saroglitazar (ZY1H) as compared to fenofibrate in patients with dyslipidemia. [Prospective Randomised Efficacy and Safety of Saroglitazar (PRESS X)]. Principal Investigator: R. H. Jani.URL: www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=6705 (published 2014). (date accessed 10/11/2014).

Author contributions
S.C. was involved in designing the study, data entry with analysis and writing of manuscript. A.M. and S.R. were involved in data collection and entry. All authors reviewed the manuscript.

Additional information
Competing financial interests: The authors declare no competing financial interests.

How to cite this article: Chatterjee, S., Majumder, A. & Ray, S. Observational Study of Effects of Saroglitazar on Glycaemic and Lipid Parameters in Indian Patients with Type 2 Diabetes. Sci. Rep. 5, 7706; DOI:10.1038/srep07706 (2015).

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerives 4.0 International License. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder in order to reproduce the material. To view a copy of this license, visit http://creativecommons.org/licenses/by-nc-nd/4.0/