DISCUSSION

As per the IDF estimates, in 2017 the global prevalence of IGT is 7.3% and a number of people with IGT 352.1 million and projected to increase to 532 million in 2045. [4] On the other hand, ICMR India Diabetes study done by Anjana et al., (2017) estimates India has presently 10.3 % prediabetes patients. [5] Earlier diseases were common in the fourth decade of life but now is frequently seen in adolescents and younger children. [55]

Chronic hyperglycemia is an important predictor of the development of diabetic complications like microvascular, macrovascular and acute metabolic complications. Chennai urban population study (CUPS) and the Chennai Urban Rural Epidemiology Study (CURES) provided valuable data from India on diabetic complications. [273,274] Diabetes is known to reduce life expectancy by a decade. Devastating complications develop despite treatment, in most sufferers. The Life-long burden imposed on individuals by diabetes is heavy. The costs to individuals and for health care are huge. Thus, any measure that could reduce the burden of diabetes is of importance socially, politically and economically. [275]

The Diabetes Prevention Program (DPP) was a 27-center randomized clinical trial to determine that both the lifestyle intervention and pharmacological therapy (metformin) were effective in preventing or delaying the onset of diabetes in individuals with impaired glucose tolerance (IGT) who are at high risk for the disease. Whereas, lifestyle intervention decreased the incidence of type 2 diabetes by 58% compared with 31% in the metformin-treated group. [276]

According to Diabetes Control and Complications Trial (DCCT) and UK Prospective Diabetes Study Group (UKPDS) revealed that adequate treatment aiming at early control of hyperglycemia is important for the reduction in these complications. It has further suggested that early diagnosis for people with prediabetes is much more cost-efficient than providing treatment only after the development of type 2 diabetes. [283] Results from the recent study provide ample evidence for the beneficial effects of early intervention to improve outcomes in prediabetes. [277]
Insulin resistance and relative insulin deficiency contribute to the pathogenesis of prediabetes. Insulin resistance, which plays a major role early in the evolution of the disease, is associated with clusters of cardiovascular risk factors like hypertension and dyslipidemia that contribute to increased risk for coronary heart disease. \[278\]

The objectives for management of prediabetes include not only normalization of hyperglycemia, but also reduction of complication associated with insulin resistance. Directly targeting underlying insulin resistance in the periphery is a relatively new approach for treating prediabetes and type 2 diabetes. Beyond enhancement in glycemic control, reduction of insulin resistance may confer beneficial changes in additional components of insulin resistance syndrome, independent of improvements in glucose metabolism. Thus, oral antihyperglycemic medication therapies that target elevated insulin resistance are rational treatment strategies that also improve the cardiovascular risk profile. \[279\]

Metformin commonly used as anti-hyperglycemic drug in the treatment of diabetes. The exact mechanism of biguanides metformin is activation of AMP-dependent protein kinase (AMPK) mediating the actions which include: Decreased basal and postprandial plasma glucose, it basically act by reducing hepatic output of glucose; increases peripheral utilization of glucose; reducing intestinal absorption of glucose; increases insulin sensitivity, reduced fatty acid oxidation; reduced weight gain and appetite; increased efficient action of glucose transporters (GLUT 4); and increased insulin-mediated insulin receptor tyrosine kinase activity. \[280\] In addition, activates AMPK, which in turn decreases mammalian target of rapamycin (mTOR) complex levels, playing the main role in governing cell growth, production, and breakdown which act as an anticancer agent. \[26\] Increases plasma levels of glucagon-like peptide 1 (GLP-1) which is a member of the incretin family of peptide hormones which is released from the gut in response to ingested glucose thereby leading to retardation of gastric emptying, inhibiting glucagon release from α cell, and produces a feeling of satiety. Side effects are abdominal pain, anorexia, bloating, nausea, metallic taste, mild diarrhea, and tiredness. Lactic acidosis is the most serious complication which is less seen with Metformin. \[27\]
Pioglitazone, insulin-sensitizing TZDs, are known to activate peroxisome proliferator-activated receptor (PPAR-γ). PPAR-γ1 is expressed in the heart, skeletal muscles, kidneys, pancreas, and epithelial tissues (urothelium and intestine). In comparison, PPAR-γ2 is expressed exclusively in adipose tissue and induces adipocyte differentiation and involved in the control of inflammatory reactions and in glucose metabolism through enhanced insulin sensitivity. PPAR-alpha seems to be expressed among various tissues, with high expression in liver, intestine, heart, and kidney. Pioglitazone enhances insulin sensitivity in the liver and peripheral organs leading to resultant glycemic control in prediabetes and T2 DM patients. It also has agonistic action of PPAR-α, activation of genes regulating fatty acid metabolism and lipogenesis in adipose tissue, results in Lipolysis and plasma fatty acid levels are reduced. Pioglitazone is dependent on the presence of insulin to exert its advantageous effects and preserve β-cells of the islets of Langerhans but does not act the same as an insulin secretagogue. Pioglitazone is well tolerated; adverse effects are plasma volume expansion or fluid retention, edema, weight gain, headache, myalgia, and mild anaemia. Few cases of hepatic dysfunction have been reported; CHF may be precipitated or worsened.

α-glucosidase inhibitors (AGI) drug like acarbose, Miglitol and Voglibose are commonly used drug to target postprandial blood glucose level. It delays the terminal stage in the digestion and absorption of carbohydrates at the brush border of the small intestine, hence lowering effect on postprandial blood glucose levels. Voglibose is a more potent and tolerant AGI as compared to Acarbose and Miglitol. This is because; voglibose selectively inhibits enzymes responsible for digestion of disaccharides but spares alpha-amylase, which is responsible for digestion of starch a polysaccharide. While acarbose also inhibits alpha amylase enzyme in addition to disaccharides causing increased amounts of starch in the small intestine. This undigested and unabsorbed starch in feces is responsible for gastrointestinal side effects (gases, flatulence, and abdominal distention).
Combination therapy for the treatment of prediabetes with an oral hypoglycaemic agent with reduced numbers of daily tablets or doses or other co-medications shows good adherence of patient with increase efficacy, bioavailability, well tolerability, dosing flexibility, and cost-effective dosage formulation with minimum side effects. Combination products are to provide rationale drug regulatory mechanism and enhance drug therapeutic effectiveness. Combination of antidiabetic agents with different mechanisms of action maintains greater glycaemic control at lower doses and fewer side effects. [284]

Consequently, the use of Combination with a complementary mechanism of action and synergistic effectiveness has become a keystone of Management of prediabetes. Combination therapy was generally well-tolerated with no increase in the incidence of hypoglycaemia because of non-pancreatic action. There was no change in body weight as well. Insulin resistance did not appear to be significantly changed and reductions in glucose triad were also observed with continues use of the combination. [285] Use of combinations of those drugs that do not cause hypoglycaemia (Metformin, Pioglitazone, Voglibose), at an early stage of the disease to achieve therapeutic HbA1c levels have also been advocated. Compliance is improved and cost lowered when multiple drugs are provided in a single tablet or capsule, and Combination of two oral hypoglycaemic agents have been available for many years. [286]

Both metformin and pioglitazone are beneficial drugs in prediabetes patients, combination of Metformin and Pioglitazone provides effective on glycaemic control by decreasing plasma glucose levels, due to decreased hepatic glucose output by inhibiting gluconeogenesis in liver and improving insulin sensitivity by increasing peripheral glucose uptake and utilization by up-regulating expression of glucose transporter (GLUT-4) and enhance insulin signalling and thereby reducing insulin resistance. [288] Moreover Combined action of Metformin with Pioglitazone was the strongest predictor for reduced risk of conversion to diabetes by preserving the function of β-cell of islets of Langerhans and ameliorate insulin resistance. [288] In the PROactive has shown that pioglitazone can significantly reduce the risk of secondary macrovascular events in a very high-risk patient population with established macrovascular disease. [57]
Furthermore, Combined treatment with Metformin and Voglibose have an impact not only on parameters of hyperglycemia mediated via traditional above-mentioned mechanism but also on entero-insular axis. Combination of Metformin and Voglibose has synergistic effect on glycemic control in prediabetes patients and combining drugs provides an advantage in terms of maximizing treatment adherence, submaximal dose, reducing toxicity. \cite{287} Metformin and Voglibose and combination of both are producing a synergistic effect on glycaemic control by decreased intestinal absorption of glucose, resulting in lowering postprandial blood glucose. \cite{53} Metformin and Voglibose combination increases Glucagon-like peptide1 (GLP-1) is an incretin hormone, which is released from the intestine following a meal. It exerts glucose-dependent insulinotropic action in \( \beta \)-cells, inhibits the secretion of glucagon and restores \( \beta \)-cell mass. \cite{287}

But there was no head to head studies comparing Metformin and Voglibose versus Metformin and Pioglitazone combination. Therefore, this study was undertaken to evaluate the efficacy and safety of Metformin and Voglibose combination versus Metformin and pioglitazone patients with prediabetes - FBG, PPBG, HOMA –IR, HbA1c levels, Serum Insulin and Lipid Profile.

Results from after 6 months of assessment of efficacy and safety in Group A (Metformin +Voglibose) and Group B (Metformin + Pioglitazone) following were outcomes.

**Effect on Fasting Blood Glucose:**

In Group A: Fasting Blood Glucose (FBG) was decreased in mean baseline value from 103.14±3.38 to 80.85±7.51 mg/dl after 6 months of treatment. The reduction of FBG was statistically significant after 6 months (\( p<0.0001 \)). In an observational GLOBE study done by *Kala et al.*, the combination treatment with Voglibose and Metformin has shown a significant reduction in FBG from 130.5 mg/dl to 119 mg/dl. \cite{287}
On the other hand, Group B: FBS was decreased in mean baseline value from 104.15±5.59 to 78.47±7.15 mg/dl after 6 months of treatment. The reduction of FBG was statistically significant after 6 months (p<0.0001). According to Sohrvardi et al. reported a significant reduction in FBG with a combination of Pioglitazone with Metformin. [288]

Intergroup comparison using unpaired t-test showed a reduction in FBG in Group A Vs Group B, i.e mean difference from baseline to after 3 months was -10.73 Vs -14.22 and baseline to after 6 months was -22.29 Vs -25.67. Hence, the mean difference change from baseline to after 3 months and baseline to after 6 months was statistically significantly reduced in Group B when compared with Group A.

**Effect on Postprandial blood glucose:**
In our study for the parameter postprandial blood glucose (PPBG) was decreased mean baseline value from 174.85±15.22 to 124.08±9.96 mg/ dl after 6 months of treatment with Group A. Metformin and Voglibose combination are produce synergistic effect on glycaemic control by decreasing intestinal absorption of glucose, resulting in lowering postprandial blood glucose and Metformin increases insulin sensitivity, increase GLUT-4 expression, increase peripheral utilization of glucose. [289]

Furthermore, Group B: PPBS was decreased in mean baseline value from 174.44±16.62 to 146.59±16.83 mg/dl after 6 months of treatment. The reduction was statistically highly significant in two groups (P < 0.0001).

The reason for the above findings could be due to the effectiveness of combination of Metformin and Pioglitazone shows glycaemic control by decreasing plasma glucose levels, due to decreased hepatic glucose output by inhibiting gluconeogenesis in liver by Metformin, and Pioglitazone improves insulin sensitivity by increasing peripheral glucose uptake and utilization by up-regulating expression of glucose transporter (GLUT-4). [290]
When a comparison was done in two groups using an unpaired t-test, reduction in PPBS in Group A Vs Group B, i.e mean difference from baseline to after 3 months was -21.08 Vs -13.32 and baseline to 6 months was -50.76 Vs -22.44. Henceforth, Group A was highly significantly reduced from baseline to after 3 months and baseline to after 6 months against Group B.

**Effects on HOMA-IR:**
Both groups showed a significant reduction in HOMA-IR level at the end of the study period. Whereas, after six months of treatment in Group A: Mean HOMA-IR reduced from 3.82±0.63 to 2.38±0.44 (-1.44, p<0.0001). Vander MP. et al showed mean HOMA-IR reduction from baseline. (-1.0, p< 0.02) with metformin which is comparable with our study. [291]

Whereas, in Group B mean HOMA-IR decreased from 3.87±0.67 to 2.12±0.39 (-1.74, p<0.0001) which was statistically highly significant in both groups (p< 0.0001). Sohrevardi Y. et al revealed that a combination of Metformin and Pioglitazone decreased fasting serum insulin level. [288]

The Study was closely related to waning β-cell function as determined by the insulin secretion/insulin resistance (IS/IR) index and that an improved IS/IR index with the combined action of Metformin with Pioglitazone was the strongest predictor for reduced risk of conversion to diabetes by preserving the function of β-cell of islets of Langerhans. [293]

When a comparison was done in two groups using an unpaired t-test, reduction in HOMA-IR in Group A Vs Group B, i.e mean difference from baseline to after 3 months was -0.65 Vs -1.00 and baseline to 6 months was -1.44 Vs -1.74. However, the mean difference change from baseline to after 3 months and baseline to after 6 months was statistically significantly reduced in Group B when compared with Group A.
Effects on HbA1c:
There was a statistically highly significant difference among the two-treatment group in HbA1c changes from baseline. Group A had significantly decreased from a baseline of HbA1c from 6.25±0.14 to 5.31±0.19 (-0.94, p < 0.0001) after six months of treatment. Voglibose in combination with metformin has been shown to improve HbA1c. It has been reported by Krishna Murti et al. that the combination of Voglibose and Metformin in sub-optimally controlled patients reduced HbA1c by about 0.7-1.0%. [294]

Metformin and Voglibose combination increases Glucagon-like peptide1(GLP-1) is an incretin hormone, which is released from the intestine following a meal. It exerts glucose-dependent insulinotropic action in β-cells, inhibits the secretion of glucagon and restores β-cell mass and add on effect of Metformin, suppresses hepatic gluconeogenesis and glucose output from the liver resultant reduction of HbA1c. [289]

Moreover, in Group B had significantly decreased from baseline in HbA1c from 6.24±0.14 to 5.14±0.11 (-1.09, p < 0.0001) after six months of treatment. Our finding is supported by Mandeep Kaur et al. study which showed a statistically significant reduction in HbA1c (-0.85%) with Pioglitazone and Metformin. [295]

The effect of combined drugs Metformin and Pioglitazone improves hepatic and peripheral insulin sensitivity, thereby inhibiting hepatic gluconeogenesis and increasing peripheral and splanchnic glucose uptake. Due to their different sites of action and different cellular mechanisms, this combination attains a potential synergistic effect on decreasing in HbA1c. [293]

When a comparison was done in two groups using an unpaired t-test, reduction in HbA1c in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –0.44 Vs -0.61 and baseline to 6 months was -0.94 Vs -1.09. However, the mean difference change from baseline to after 3 months and baseline to after 6 months was statistically significantly reduced in Group B when compared with Group A.
**Effects on Serum Insulin:**

Both groups showed a significant reduction of serum insulin level at the end of the study period. Whereas, after six months of treatment in Group A mean serum insulin decreased from 15.01±2.40 to 11.94±1.90 (-3.07, p<0.0001). With respect to a study done by Deepak Bhosle et al. our finding is similar to his study, in Voglibose with Metformin, mean Serum Insulin was statistically significantly reduced. \[296]\n
Voglibose treatment has resulted in an increased release of GLP-1, which is an insulinotropic hormone and it has also known to enhance insulin release from pancreatic β cells and enhance insulin sensitivity add on effect of Metformin also sensitize of insulin in peripheral tissues; and increased the insulin-mediated insulin receptor activity. \[287]\n
In Group B mean serum insulin from 15.05±2.40 to 10.97±1.67 (-4.08, p <0.0001) which was statistically highly significant in both groups (p< 0.0001). According to Mandeep Kaur et al. significant fall of serum insulin level with Pioglitazone and Metformin. \[295]\n
Combination of drugs such as Metformin and Pioglitazone demonstrate improved β cell function and ameliorate insulin resistance than either drug alone. Both drugs improved glycaemic control in prediabetes by increasing insulin sensitivity by increasing peripheral glucose uptake and utilization. The result of these interaction includes increased in glucose transporters 4 (GLUT4), enhance insulin signalling and thereby reducing insulin resistance. \[293]\n
When a comparison was done in two groups using an unpaired t-test, reduction in Serum Insulin in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –1.13 Vs -2.07 and baseline to 6 months was -3.07 Vs -4.08. However, the mean difference change from baseline to after 3 months and baseline to after 6 months was statistically significantly reduced in Group B when compared with Group A.
Effect on Lipid profile:
Similarly, two groups showed a significant reduction in Lipid profile at the end of 6 months. In our study Group A: Total cholesterol level was decreased from baseline value 285.97 ± 11.05 to 267.40 ± 15.00 mg/dl after 6 months of treatment. On the other hand, Group B: Mean Total cholesterol was decreased in mean baseline value from 285.89 ± 9.88 to 261.55 ± 15.92 mg/dl after 6 months of treatment.

In our study Group A: Serum Triglycerides level was decreased from baseline value 189.94 ± 7.52 to 175.17 ± 8.66 mg/dl after 6 months of treatment. Furthermore, Group B: Serum Triglycerides was decreased in mean baseline value from 189.37 ± 10.67 to 170.10 ± 11.54 mg/dl after 6 months of treatment.

In Group A: HDL cholesterol level was increased from baseline value 41.13 ± 1.89 to 44.92 ± 2.44 mg/dl after 6 months of treatment. Moreover, in Group B: HDL cholesterol level was increased in mean baseline value from 41.23 ± 1.36 to 46.17 ± 2.08 mg/dl after 6 months of treatment.

In Group A: LDL cholesterol level was decreased from baseline value 206.84 ± 11.28 to 187.44 ± 14.88 mg/dl after 6 months of treatment. In addition, in Group B: LDL cholesterol was decreased in mean baseline value from 206.78 ± 10.17 to 181.56 ± 16.66 mg/dl after 6 months of treatment.

In Group A: VLDL cholesterol level was decreased from baseline value 37.98 ± 1.50 to 35.03 ± 1.73 mg/dl after 6 months of treatment. On the other hand, in Group B: VLDL cholesterol was decreased in mean baseline value from 37.87 ± 2.13 to 34.02 ± 2.30 mg/dl after 6 months of treatment. According to a study done by Amita Jindal et al., Voglibose and pioglitazone in combination with Metformin, there was decreased level of TC, TG, LDL, VLDL and improves HDL levels, which support with our study. [297]

When a comparison was done in two groups using an unpaired t-test, reduction in Total Cholesterol in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –9.44 Vs -13.64 and baseline to 6 months was -18.56 Vs -24.34.
Reduction in Triglycerides in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –7.76 Vs -11.08 and baseline to 6 months was -14.76 Vs -19.26.

Increase in HDL level in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –1.97 Vs -2.77 and baseline to 6 months was -3.79 Vs -4.94.

Reduction in LDL level in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –9.86 Vs -14.20 and baseline to 6 months was -19.40 Vs -25.22.

Reduction in VLDL level in Group A Vs Group B, i.e mean difference from baseline to after 3 months was –1.55 Vs -2.21 and baseline to 6 months was -2.95 Vs -3.85.

However, a mean difference change from baseline to after 3 months and baseline to after 6 months was statistically significantly reduced in Group B when compared with Group A.

Moreover, metformin-induced insulin-stimulated glucose disposal in the skeletal muscle, reduction in appetite and anorectic component, decrease in leptin levels, and rise in GLP-1 levels with Metformin and voglibose contribute to improving dyslipidaemia. [298]

Pioglitazone control dyslipidemia (lowers TC, TG, LDL, VLDL and raises HDL level) in prediabetes patients through agonist of PPAR- \( \alpha \). PPAR in adipose tissue reduces the flux of fatty acid into muscle, thereby lowering insulin resistance. It also causes activation of adiponectin which leads to increases insulin sensitivity by elevating AMP kinase, which stimulates glucose transport into muscle and increases fatty acid oxidation. Because both metformin and Pioglitazone apparently converge on AMP kinase this is a very important target for drug development. [299] These agents mobilize fat from muscle and liver thereby improving lipotoxicity. PPAR is significantly lower in visceral (omentall) fat by mobilization of visceral fat to subcutaneous fat. The potential synergistic impact of combined therapy of **Metformin and Pioglitazone** both reduced lipogenesis in adipose tissue and enhanced fatty acid oxidation. [300] To
conclude, delay of diabetes from the prediabetes condition, pioglitazone also prevents the progression of atherosclerosis in these patients, thus reducing the risk of coronary artery diseases.

In our study, the most common adverse drug reaction reported in the two groups were related to gastrointestinal disturbances. In Group A, gastrointestinal adverse drug reactions were: Nausea in 3 (4.4%) patients, Abdominal blotting in 5 (7.4%) patients, Flatulence in 7 (10.4%) patients, Diarrhea in 4 (5.9%) patients, Abdominal pain in 5 (7.4%) patients.

On the other hand, in Group B gastrointestinal adverse drug reactions and headache experienced by patient, Nausea in 2 (2.9%) patients, Abdominal blotting in 4 (5.9%) patients, Diarrhea in 3 (4.4%) patients, and Abdominal pain in 4 (5.9%) patients and weight gain in 6 (8.9%). While comparing both groups, in Group B had minimal side effects, thereby showing that pioglitazone is a safer drug. No treatment was needed for this side effect in both groups.

The mechanism of GI intolerance caused by metformin are different hypothesis includes stimulation of intestinal secretion of serotonin, alteration in incretin and metabolism of glucose, and malabsorption of bile salts. It has been found that metformin structure has some similarities with 5-hydroxytryptamine (5-HT) receptor-selective agonists and, is transported by Serotonin Reuptake Transporter (SERT). The release of serotonin (5-hydroxytryptamine (5-HT)) from the intestine results in the symptoms nausea, vomiting and diarrhoea which are similar to those as linked with metformin intolerance. Within the intestine, the bile acid pool is increased by metformin, mainly through decreased ileum absorption. This could also account for metformin intolerance through changes in the microbiome and stool consistency which in turn causes flatulence. Whereas, with Voglibose, Gastro Intestinal side effect is mainly caused by unabsorbed carbohydrates in the gut. Pioglitazone causes weight gain, due to the stimulation of preadipocyte differentiation into mature fat cells and causes induction of lipogenesis through PPAR-γ and redistribution visceral fat to subcutaneous fat, resulting in an increase in whole-body adiposity.
Finally, results of our study confirm that when the values of both the groups after 6 months of therapy were compared by unpaired t-test, there was a statistically significant different in both groups, the levels of FBS, PPBG HOMA-IR, HbAlc, Serum insulin and lipid Profile showed a statistically highly significant difference. But when percentage reductions of FBS, HOMA-IR, HbAlc, Serum insulin and Lipid profile were more in Group B compared with Group A. This shows that Metformin and Pioglitazone are more efficacious, safest than Voglibose group.

Furthermore, both metformin and pioglitazone have a complementary mechanism of action which have been revealed to improve glycaemic control and improve insulin sensitivity. Metformin increases the sensitivity of insulin over activation of AMPK in the liver; pioglitazone also increases the sensitivity of insulin over activation of PPAR-γ in adipocytes. Owing to diverse sites of action and diverse cellular mechanisms, the combination leads to a reduction in HbA1c and has synergistic and add on effect on the resistance of insulin. Whereas resistance of insulin prevails in prediabetes, insulin-sensitizing drugs signify worthwhile management preference. The latest study has revealed pioglitazone reduces the content of hepatic fat in prediabetes and increases the sensitivity of hepatic insulin. \(^{[303]}\) Pioglitazone usage causes an increase in weight, on the other hand, metformin usage causes loss of weight. Loss of weight in prediabetes patient, usage with metformin has revealed in most of the earlier research. \(^{[303]}\)

Furthermore, this combination improves the three-key pathologic condition associated with prediabetes: Improve β-cell function, decreased insulin resistance and increased hepatic glucose output.

An important concern with the use of combination therapies compared to monotherapy is increased incidences of adverse events seen in Monotherapy. \(^{[303]}\) However, this study showed that both Metformin and Voglibose and Metformin and Pioglitazone are generally well tolerated. The low incidence of hypoglycaemia seen in this study with Metformin and Voglibose combination despite the marked improvement in glycaemic control. The incidences of overall gastrointestinal adverse experiences and the specific adverse experiences of flatulence, nausea, vomiting, abdominal pain were seen in Metformin and Voglibose. However, significantly lower
incidences of diarrhoea and abdominal discomfort were seen with Metformin and Pioglitazone.

Finally, Combination of oral pharmacological preparations with two or more than two drugs in a one preparation increase efficacy, dosing flexibility, ease of administration, convenience, decreases medication load and economy. The main aim of prediabetes management is to attain good glycaemic control and to decrease prediabetic condition, retard micro and macrovascular complaints. Prediabetes patients globally increased doubled in the following 20 years, leading to complication like hypertension and obesity. Hence, the expansion of anti-diabetic combination in one medication can decrease economic load which offers a cost-effectiveness medication without extra pills. Combination of drugs or polypills, when administered in the early onset of the disease, might help in improving therapeutic outcomes in prediabetes and prevent complications.