Effects of Glibenclamide and Glimepiride Compared in Type II DM Patients in Accordance with Lipid Parameters, ESF and Glycated Haemoglobin

K. Chandra Mouli Krishna¹, B. Sowmya², Bandopadhyay Mamata³ and M. Prasad Naidu⁴*

¹NRI Institute of Medical College, Sangivalasa, Visakhapatnam -531162, Andhra Pradesh, India.
²Kamala Nursing Home, Marripalem, Visakhapatnam - 530018, Andhra Pradesh, India.
³Department of Pharmacology, Maharaja Institute of Medical Sciences, Nellimarla, Vizinagaram - 535217, Andhra Pradesh, India.
⁴Department of Biochemistry, Narayana Medical College and Hospital, Nellore-524003, Andhra Pradesh, India.

Authors’ contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

The population of Indian adults suffering from diabetes is expected to increase threefold, from 19.4 million in 1995 to 57.2 million in 2025. The objective of the study was to evaluate the efficacy and safety of antidiabetic drug and to find out their cardio protective action in patients with diabetes mellitus. In all, 60 patients who were newly diagnosed with Type II diabetes mellitus or who were already on treatment for Type II diabetes mellitus were enrolled in our study. The study was conducted on patients suffering from Type II diabetes mellitus for a period of 6 months from December 2011 to June 2012. These were patients attending the Medical and Surgical OPD’s of Maharajah’s Institute of Medical Sciences (MIMS) Hospital, Nellimarla, Vizianagaram district,
1. INTRODUCTION

Diabetes, with its associated acute and long-term complications, and the myriad of disorders associated with it, is a major health hazard [1]. In keeping with the scenario of most developing countries, India has long passed the stage of a diabetes epidemic [2]. The problem has now reached, in scientific language, "pandemic" proportions. To put it simply, it has crossed the dividing line in which it is a problem associated with individuals, no matter how large this number may be, and is now a problem in public health of a large magnitude, growing astronomically each year. More than a matter of individual health and well being, the pandemic calls for an effort in which attention must be paid in bringing social awareness [3]. Recent WHO (World Health Organization) projections suggest that the number of adults suffering from diabetes in India is expected to increase threefold, from 19.4 million in 1995 to 57.2 million in 2025 [4]. Presently it is 50.8 million in 2010. It has been confirmed that between 10% to 12% of urban population and 4% to 6% of rural population of India have diabetes now [5].

Diabetes mellitus is characterized by hyperglycemia, altered metabolism of lipids, carbohydrates & proteins; and an increased risk of complications from vascular disease [6]. Diabetes mellitus will eventually cause cardiac, vascular, renal, hematological, ocular, neuronal complications and will result in end organ failure [7]. The standard of care therapy available for diabetes mellitus is insulin and oral hypoglycemic drugs. FBS (Fasting Blood Sugar) and HbA1c (Glycated Hemoglobin) are now the most important parameters for diagnosis and management of diabetes [8].

Patients with diabetes mellitus are primarily receiving insulin or anti-diabetic drugs with hypoglycemic therapy as the dominant aim, but the pathogenic endogenous changes due to diabetes mellitus occur from the onset of hyperglycemic condition, in which very commonly the atherosclerogenic risky lipid profile features gradually develop in spite of good glycemic control [9]. The lipid profile is a very important prognostic marker for diabetes mellitus complicated with cardiovascular manifestations such as atherosclerosis, myocardial infarction, decreased peripheral circulation and gangrene, stroke, and neurovascular complications, etc. Thus assessing the lipid profile parameters like LDL (Low Density Lipoprotein), VLDL (Very Low Density Lipoprotein), and HDL (High Density Lipoprotein) from the point of diagnosis of diabetes is very much essential, such that the care of the patients increases and subsequently leading to a decrease in various type of complications [10].

The Efficacy variables taken in this study were percentage decrease in FBS, HbA1c, TC (Total Cholesterol), TG (Triglycerides), LDL, VLDL and the percentage increase in HDL, ESF (Ejection systolic fraction) and Hb% (Hemoglobin Percentage) over 12 weeks period. The Safety variables, adverse drug reactions of anti-diabetic drugs, hematological, laboratory and clinical parameters were monitored over the period of study [11]. The aim of this study is to evaluate the cardio protective effects of Glibenclamide and Glimepiride in Diabetes Mellitus patients and the objective of the study was to evaluate the efficacy and safety of these drugs.

2. MATERIALS AND METHODS

2.1 Objects

Patients were prescribed with a starting dose of 5 mg of Glibenclamide, 1 mg of Glimepiride and 500 mg of Metformin orally, which was minimum...
required dose at which subjects showed clinical improvement. If no clinical or hematological response, the dose was escalated to a maximum of 10 mg Glibenclamide, 4 mg of Glimepiride and 1000 mg of Metformin, once in 2 weeks. Patients were supplied with the drug on a weekly basis and were requested to return the unused tablets. After obtaining informed consent, the patients were randomly allocated to group. On the initial contact, the demographic data, clinical history and physical examination of the patient were noted.

2.2 Sample Collection

Standard diagnostic laboratory procedures were implemented in the sample collection and estimation of the dependent variables for all the patients of both the groups. Baseline laboratory investigations like Estimation of Hb% by using Hemoglobinometry (Sahli’s Method), determination of FBS by using Glucose oxidase peroxidase method (GODPOD Method), estimation of HbA1c by using Chromatography based HPLC assay. The study was conducted for a period of 6 months during the period of December 2011 to June 2012, on patients suffering from Type II Diabetes Mellitus attending the Medical and Surgical OPD’s of Maharajah’s Institute of Medical Sciences (MIMS) Hospital, Nellimarla, Vizianagaram district, Andhra Pradesh.

2.3 Lipid Profile Measurement

Human Analyzer kits to analyze Total cholesterol, triglycerides and HDL, and LDL. VLDL-cholesterol is calculated by Friedwald’s formulae.

2.4 Cardiac Function Analyses

Observation of ECG by Standard 6 – Lead Electrocardiography and Ejection Systolic Fraction by using 2D Echocardiography methods were done.

2.5 Inclusion Criteria

Both Male & Female between the ages of 20 to 70 years with Type II DM patients who were recently diagnosed and who were already on treatment are included in the study.

2.6 Exclusion Criteria

The patients with Type I DM, with sever debilitating diseases like renal failure and cardiovascular diseases, Myocardial Infarction, recent infections, major surgeries and irregular dietary habits have been excluded in this study. The objective of the study was to evaluate the efficacy of Glibenclamide and Glimepiride in cardiac protection and to evaluate the safety of these drugs.

Patient was asked to come for follow-up on weekly basis and outcome variables were reassessed if felt necessary on examination. At the time of enrollment every patient was given a green colored follow-up card, on which were written his name, enrollment number, identification number, address, group to which he belonged and date of next follow up. Patients from both the groups either continued with their respective treatment regimens or were put on standard anti-diabetic therapy depending on the efficacy and safety of the treatment regimens at the discretion of the clinician. ECG and Ejection Systolic Fraction values were reviewed by the investigator and even by the consultant Cardiologist of MIMS Hospital. All the obtained results were tabulated and compared using Student "t" test and graphical representation was done accordingly.

The approval of Ethics committee (IEC) of MIMS was taken before the start of the study. Total 60 patients who were newly diagnosed with Type II diabetes mellitus or who were already on treatment for Type II diabetes mellitus were enrolled in our study.

3. RESULTS

The present study was conducted in the Department of Pharmacology, Maharajah’s Institute of Medical Sciences (MIMS), Nellimarla, Vizianagaram during the period of December 2011 to June 2012 for 6 months. Sixty patients of Type II diabetes mellitus ranging from 18 to 70 years age group were considered as subjects for the study. Therapeutic Group – 1 were kept on Tab. Glibenclamide 5 mg to 10 mg + Metformin 500 mg to 1000 mg. Group – 2 were kept on Tab. Glimepiride 1 mg to 4 mg + Metformin 500 mg to 1000 mg for a period of 12 weeks. At the end of the study the following observations and results were obtained.
Fig. 1: Results of Dependable Variables before and after administration of Glibenclamide + Metformin Drug Therapy. Fig. 2: Results of Dependable Variables before and after administration of Glimepiride + Metformin Drug Therapy. Estimation of Dependable Variables was done at the beginning i.e. at the enrollment and again after 3 months of drug therapy. Estimations of Hb%; FBS; HbA\(_{1C}\); Lipid Profile \(\rightarrow\) TC, TG, HDL, LDL, VLDL; ECG and Ejection Systolic Fraction (ESF) were done and compared. The mean values of both the group are noted.

Using the frequency intervals and frequency of range, bar diagram was prepared for the mean values of both Glibenclamide + Metformin therapy (Group \(-\) 1) and Glimepiride + Metformin therapy (Group \(-\) 2). [Values from the above Table (5)]

**Group \(-\) 1:** The difference of mean values of Hb% is 0.764 gm%; indicating a minimal rise in the level of Hb% after 3 months of drug therapy. The difference of mean values of FBS is 8.3 mg/dl; indicating a mean decrease in the level of FBS after 3 months of drug therapy. The difference of mean values of HbA\(_{1C}\) is 0.1 mmol/l; indicating a mean minimal decrease in the level of HbA\(_{1C}\) after 3 months of drug therapy. The difference of mean values of lipid profile indicated a fall in their levels after 3 months of drug therapy. The difference of mean values of ESF is 0.5%; indicating a minimal rise in the level of ESF after 3 months of drug therapy.

Above bar diagram shows pretreatment values of Hb% have decreased comparatively after treatment.

The null hypothesis is rejected at the 0.05 level of significance and one star (*) result in tables.

| Symbol | Meaning         |
|--------|-----------------|
| ns     | \(P > 0.05\)    |
| *      | \(P \leq 0.05\) |
| **     | \(P \leq 0.01\) |
| ***    | \(P \leq 0.001\) |
| ****   | \(P \leq 0.0001\) (see note) |

This is fairly standard, but not completely, stars expressed figures
**Group – 2:** The difference of mean values of Hb% is 0.4 gm%; indicating a minimal rise in the level of Hb% after 3 months of drug therapy. The difference of mean values of FBS is 30.2 mg/dl; indicating a mean decrease in the level of FBS after 3 months of drug therapy. The difference of mean values of HbA1C is 0.4 mmol/l; indicating a mean decrease in the level of HbA1C after 3 months of drug therapy. The difference of mean values of TC is 24 mg/dl; indicating a fall in the level of TC after 3 months of drug therapy. The difference of mean values of TG is 16.1 mg/dl; indicating a fall in the level of TG after 3 months of drug therapy. The difference of mean values of HDL is 0.7 mg/dl; indicating an increase in the level of HDL after 3 months of drug therapy. The difference of mean values of LDL is 16 mg/dl; indicating a fall in the level of LDL after 3 months of drug therapy. The difference of mean values of VLDL is 3.13 mg/dl; indicating a fall in the level of VLDL after 3 months of drug therapy. The difference of mean values of ESF is 1.13%; indicating a minimal rise in the level of ESF after 3 months of drug therapy.

Table 1: Unpaired samples statistics of the Pre – treatment values of both the Groups 1 & 2 (in between the two groups). Table 2: Paired samples statistics of Group – 1 (Glibenclamide + Metformin drug therapy) with in the same group. Table 3: Paired samples statistics of Group – 2 (Glimepiride + Metformin drug therapy) with in the same group. Table 4: Unpaired samples statistics of the Post –treatment values of both the Groups 1 & 2 (in between the two groups).

| Age distribution | Group 1 | Group 2 | Total |
|------------------|---------|---------|-------|
| 20–35            | 4       | 8       | 12    |
| 36–45            | 6       | 6       | 12    |
| 46–55            | 7       | 7       | 14    |
| 56–65            | 6       | 4       | 10    |
| 66–70            | 7       | 5       | 12    |
| Total            | 30      | 30      | 60    |

| Sex             | Group 1 | Group 2 | Total |
|-----------------|---------|---------|-------|
| Male            | 26      | 19      | 45    |
| Female          | 4       | 11      | 15    |
| Total           | 30      | 30      | 60    |

| Pre Rx values of groups | Mean±SD | p value |
|-------------------------|---------|---------|
| Hb                      | 9.966±1.425 | 0.866  |
| HbA1C                   | 7.450±0.854 | 0.392  |
| FBS                     | 120.50±28.377 | 0.286  |
| TC                      | 211.67±45.011 | 0.244  |
| TG                      | 224.03±35.807 | 0.244  |
| HDL                     | 44.500±9.744 | 0.000  |
| LDL                     | 143.43±38.892 | 0.072  |
| VLDL                    | 44.566±12.353 | 0.382  |
| ESF                     | 57.433±13.366 | 0.706  |
| BMI                     | 32.644±1.834 | 0.001  |

SD – Standard Deviation; SEM – Standard Error Mean. T value is the value of Student “t” test. df – Degrees of Freedom. Pre treatment values of Group – 1 (Glibenclamide + Metformin) and Group – 2 (Glimepiride + Metformin).
Using the frequency intervals and frequency of range, bar diagram was prepared for the mean values of Pre Rx and Post Rx within Group – 1 (Glibenclamide + Metformin). [Values from the Table (4)].

### Table 4. Paired samples statistics of Group – 1 (Glibenclamide + Metformin drug therapy) with in the same group

|          | Group 1 | Mean±SD   | p value |
|----------|---------|-----------|---------|
| Hb%      | Pre Rx  | 9.966±1.425 | 0.011   |
|          | Post Rx | 10.733±0.907 |         |
| FBS      | Pre Rx  | 120.50±28.377 | 0.145   |
|          | Post Rx | 112.93±22.528 |         |
| HbA1C    | Pre Rx  | 7.450±0.858  | 0.161   |
|          | Post Rx | 7.350±0.559  |         |
| TC       | Pre Rx  | 211.67±45.011 | 0.01    |
|          | Post Rx | 188.10±37.823 |         |
| TG       | Pre Rx  | 202.27±81.291 | 0.037   |
|          | Post Rx | 192.60±71.526 |         |
| HDL      | Pre Rx  | 44.500±9.744  | 0.452   |
|          | Post Rx | 43.700±6.295  |         |
| LDL      | Pre Rx  | 143.43±38.892 | < 0.001 |
|          | Post Rx | 127.33±27.269 |         |
| VLDL     | Pre Rx  | 44.567±12.353 | 0.291   |
|          | Post Rx | 41.567±15.712 |         |
| ESF      | Pre Rx  | 57.433±13.366 | 0.01    |
|          | Post Rx | 58.033±12.729 |         |

![Fig. 2. Biochemical values pre and post treatment](image)

Above bar diagram shows pretreatment values of lipid profile have decreased comparatively after treatment.
Above bar diagram shows pretreatment values of ESF have decreased comparatively after treatment.

Table 5. Paired samples statistics of Group – 2 (Glimepiride + Metformin drug therapy) → with in the same group

|          | Group 2 | Mean±SD          | p value |
|----------|---------|------------------|---------|
| Hb%      | Pre Rx  | 10.033±1.607     |         |
|          | Post Rx | 10.433±1.072     | 0.008   |
| FBS      | Pre Rx  | 131.03±45.454    |         |
|          | Post Rx | 112.93±22.528    | 0.017   |
| HbA1C    | Pre Rx  | 7.616±0.625      |         |
|          | Post Rx | 7.216±0.485      | < 0.001 |
| TC       | Pre Rx  | 224.03±35.807    |         |
|          | Post Rx | 201.63±33.196    | < 0.001 |
| TG       | Pre Rx  | 207.70±74.710    |         |
|          | Post Rx | 192.37±69.060    | < 0.001 |
| HDL      | Pre Rx  | 37.366±3.034     |         |
|          | Post Rx | 38.066±3.352     | 0.122   |
| LDL      | Pre Rx  | 160.03±30.862    |         |
|          | Post Rx | 144.07±25.110    | < 0.001 |
| VLDL     | Pre Rx  | 41.33±15.886     |         |
|          | Post Rx | 38.20±13.993     | 0.013   |
| ESF      | Pre Rx  | 58.900±16.424    |         |
|          | Post Rx | 60.033±15.401    | < 0.001 |

Using the frequency intervals and frequency of range, bar diagram was prepared for the mean values of Pre treatment and Post treatment with in Group – 2 (Glimepiride + Metformin). [Values from the above Table (5)].
Table 6. Proportion of people reaching glycemic control goals

|                                    | Glibenclamide/ Metformin | Glimepiride/ Metformin |
|------------------------------------|--------------------------|------------------------|
|                                    | 6 months                 | 6 months               |
| Fasting glucose ≤120 mg/dl         | 45.9%                    | 46.6%                  |
| Postprandial glucose < 140 mg/dl   | 29.7%                    | 27.4%                  |
| Reduction in HbA1C ≥1%             | 78.4%                    | 75.3%                  |
| HbA1C < 7%                         | 35.1%                    | 50.7%                  |

*p < 0.05 between both groups at 6 months.

The Table 6 shows the metabolic control goals in both groups at 6 months; the glimepiride group showed the highest proportion of patients who reached the HbA1C < 7% goal at 6 months of treatment compared to glibenclamide group.

5. DISCUSSION

There are many studies about the health of the individuals who are suffering from Diabetes Mellitus with underlying endogenous risky changes leading to various complications like cardiovascular disorders but the mortality rate among Diabetes Mellitus patients is not retarding because of meager availability of exclusive anti-diabetic agent comparatively with no extra inference of cardiac protection.

Generally, the antilipidemic drugs are used whenever the signs of cardiac risk factors are well established but in case of Diabetes Mellitus the cardiac risk factors are associated with hyperglycemic effect. Hence, a parallel glycemic control & cardio protective measure is of utmost importance. Glibenclamide/metformin is the oral antidiabetic combination most used in the clinical practice previously; on the other hand, glimepiride—considered as a third-generation sulfonylurea agent—has several beneficial pharmacological effects over glibenclamide, a second-generation sulfonylurea. Clinical trials support the use of combinations of antidiabetic agents with complementary mechanisms of action such as a sulfonylurea/metformin. Early aggressive treatment could improve patient outcomes while reducing overall health care costs.

The antidiabetic drugs, besides being hypoglycemic agents also found to have an influence on lipid profile features as a cardio protective measure. A tendency to decrease total cholesterol, Triglycerides, LDL, VLDL and an increase in HDL values are considered to be one of the cardio protective effects. So a concern to study for the search of a selective, exclusive anti-diabetic agent (in combination therapy with Metformin) for additional effects like cardio-protective measure keeping in view the lipid profile features mainly and other features like ECG, Ejection systolic fraction, FBS, HbA1C and Hb%, were considered.

Following the methodology, proper estimation of the efficacy variables was done following the safety measures and by standard laboratory methods in this study, which had shown that there was no significant difference in the baseline characters (Pre Treatment values) in both the groups (Table – 1), like there was no significant difference Hb%; FBS; HbA1C; TC; TG; LDL; VLDL and ESF values. There was a significant difference in the HDL values – the mean HDL value of group 1 was 44.5 mg/dl and group 2 was 37.36 with a p = < 0.001. This indicates that both the groups are nearly similar.

Except for the mean values of TC, TG, LDL, ESF and Hb% there was no significant difference in the Post Rx values with Glibenclamide 5 mg to 10 mg + Metformin 500 mg to 1000 mg for a period of 12 weeks (Group – 1). There was a significant difference in the Post Rx mean values of FBS, HbA1C, TC, TG, LDL, VLDL, ESF and Hb% (except HDL) with Glimepiride 1 mg to 4 mg + Metformin 500 mg to 1000 mg for a period of 12 (Group – 2). This study indicated a significant decrease in FBS, HbA1C, TC, TG, LDL, VLDL and a significant increase in Hb% & ESF, and there was an increase in HDL value but not significant with Group – 2 (Glimepiride + Metformin) when compared to Group – 1 (Glibenclamide + Metformin).

This study results correlate better with the study done by R. D. Shimpi et al, who have done for 12 weeks and both these studies show Metformin-glimepiride combination can be considered as the best combination in patients with increased lipid profile parameters as compared to metformin-glibenclamide combination in diabetic patients.
When compared with Manuel González-Ortiz et al study, who have taken the same drug combinations and studied for a period of 12 months where the efficacy variables being Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), FBS, Postprandial Glucose, HbA1C, HDL and Triglycerides (TG). They have got a significant decrease in HbA1C levels in the glimepiride group. While in this study, where the same drug combinations were taken for a period of 12 weeks, which had given a significant difference in FBS, HbA1C, TC, TG, LDL, VLDL, ESF and Hb% at the end of the study with lower concentrations in the glimepiride group. Both these studies have shown Metformin-glimepiride combination can be considered as the best combination in diabetic patients with increased lipid profile parameters as compared to metformin-glibenclamide.

Our results also correlate with the findings of Tsunekawa et al who studied for 8 weeks. Both the studies showed Glimepiride not only improved blood glucose metabolism and insulin resistance in peripheral tissues, but also may improve factors related to the insulin resistance syndrome, such as plasma lipid profile, and eventually Glimepiride may be expected to retard the progression of arteriosclerosis [12].

The results of this study were in comparison with the above studies where there was significant decrease in the lipid profile parameters (LDL, VLDL, TC, TG) with better improvement in Glycemic control (FBS & HbA1C) with Glimepiride + Metformin group.

Different studies showed different post treatment values of HDL. There was no difference in HDL values in both the groups of Manuel González-Ortiz et al. [13] there was a significant increase in the mean values of HDL with Glimepiride + Metformin and there was no change with Glibenclamide + Metformin in R. D. Shimpjet al study. In this study there was increase in HDL with Glimepiride + Metformin but was not significant and there was a decrease in HDL with Glibenclamide + Metformin. Hence the effect of Glibenclamide, Glimepiride and Metformin has to be evaluated thoroughly for confirmation of their effect on HDL.

6. LIMITATIONS

The major limitation of this study was the treatment duration, which was 12 weeks similar to the R. D. Shimpjet al. If the study period had been extended for another 12 weeks, HbA1C could be done at the end of 12 weeks and 24 weeks, and also the influence of the treatment on HDL might be evident. Open label study was another limitation of this study.

7. CONCLUSION

Based on the above results and discussion we conclude in the present study that both drug combinations i.e., Glimepiride + Metformin and Glibenclamide + Metformin have reduced the Glycated Hemoglobin level significantly, but Glimepiride + Metformin combination had given a greater control of glucose levels compared with Glibenclamide + Metformin. The significant reduction in the total cholesterol, serum triglyceride and Low density lipoprotein cholesterol was observed with Glimepiride + Metformin. It had also increased the High density lipoprotein cholesterol level which was not observed with Glibenclamide + Metformin over a study period of 12 weeks. This clearly indicates that Glibenclamide + Metformin has better therapeutic benefit in elevated lipid profile patients which is of superior prognostic value in Type II Diabetes Mellitus patients helping in cardiac protection. Therefore we have conclude that Glimepiride + Metformin can be taken into acceptance as a better drug combination of choice in patients with elevated levels of lipid profile as that compared to the other drug combination.

ETHICAL APPROVAL

The Institutional Ethics Committee approved the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Raison, Charles L, Andrew H Miller. When not enough is too much: the role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. American Journal of Psychiatry. (2003);160(9):1554-1565.

2. Tripathy, Tapas Brata, et al. A community based cross-sectional study: Increasing prevalence of type 2 diabetes among rural
adult population of Karnataka, India. 
Explor Anim Med Res. 2013;3:41-47.

3. Marwick Thomas H, et al. Exercise training 
for type 2 diabetes mellitus impact on 
cardiovascular risk: a scientific statement 
from the American Heart Association. 
Circulation. 2009;119(25):3244-3262.

4. Siegel Jacob S, Sally L Hoover. 
International trends and perspectives: 
Aging. Vol. 3. US Department of 
Commerce, Bureau of the Census; 1984.

5. Kumar Shuba, et al. Perceptions about 
varieties of brown rice: A qualitative study 
from Southern India. Journal of the 
American Dietetic Association. 2011; 
111(10):1517-1522.

6. Ceriello Antonio. Postprandial 
hyperglycemia and diabetes complications 
is it time to treat? Diabetes. 2005;54(1):1-7.

7. Ruggenenti Piero, et al. Preventing 
microalbuminuria in type 2 diabetes. New 
England Journal of Medicine. 2004; 
351(19):1941-1951.

8. Serban V, et al. Increasing incidence of 
childhood type 1 diabetes mellitus in 
Romania. Pediatric Diabetes. 2006;7:5.

9. Khalil Aly B, Ali S Al Zahrani, Salem A 
Beshyah. The first clinical congress of the 
gulf chapter of the American Association of 
Clinical Endocrinologists, October, 3rd-5th 
2013, St Regis Hotel, Abu Dhabi, United 
Arab Emirates. Ibnosina Journal of 
Medicine and Biomedical Sciences. 2013; 
5(6):363-402.

10. Biller Jose, Betsy B Love. Vascular 
diseases of the nervous system. Neurology 
in Clinical Practice: The Neurological 
Disorders. 2004;2:1197.

11. Marre M, et al. Improved glycaemic control 
with metformin–glibenclamide combined 
tablet therapy (Glucovance®) in Type 2 
diabetic patients inadequately controlled 
on metformin. Diabetic Medicine. 2002; 
19(8):673-680.

12. Tsunekawa Taku, et al. Cerivastatin, a 
hydroxymethylglutaryl coenzyme a 
reductase inhibitor, improves endothelial 
function in elderly diabetic patients within 3 
days. Circulation. 2001;104(4):376-379.

13. Reynoso-von Drateln Claudia, et al. Lipid 
profile, insulin secretion, and insulin 
sensitivity in psoriasis. Journal of the 
American Academy of Dermatology. 2003; 
48(6):882-885.

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