RESEARCH ARTICLE

Glucose Control in Diabetic Patients Attending Parirenyatwa Group of Hospitals in Zimbabwe

Magnus Chirombe[1], Bernard Ngara[2], Raymond Chibvongodze[1], Venneth Charuka[1] and Danai Tavonga Zhou[1,*]

[1]*Department of Medical Laboratory Sciences, College of Health Sciences, University of Zimbabwe, P.O. Box AV 178, Avondale, Harare, Zimbabwe*

[2]*Department of Community Medicine, University of Zimbabwe, P.O. Box AV 178, Avondale, Harare, Zimbabwe*

Abstract:

Background:

Diabetes mellitus is a non-communicable disease whose prevalence is increasing even in low-income countries like Zimbabwe. It is usually diagnosed late when complications are already present mainly due to slow onset of disease, low accessibility to healthcare facilities and socio-economic hardships. Poor glycaemic control in diabetics is associated with the development of long-term microvascular and macrovascular complications such as nephropathy, neuropathy, retinopathy, cardiovascular disease and diabetic foot syndrome. Therefore, good glycaemic control is essential to prevent complications, to improve the quality of life of diabetic patients and to reduce healthcare costs.

Objectives:

This study sought to find the status of glycaemic control and to identify factors that are associated with poor glycaemic control among diabetic patients attending Parirenyatwa Group of Hospitals Diabetic Clinic in Harare, Zimbabwe.

Method:

A cross-sectional study involving a total of 182 diabetic patients was carried out. Demographic data (age and gender) and clinical information (hypertension, duration, height, weight and lipid therapy) were retrieved from patients' clinical records. Blood samples from participating diabetic patients were analysed for HbA1c on the Mindray® BS 400 Analyser. Measurement of HbA1c was done enzymatically using the International Federation of Clinical Chemists (IFCC) method.

Result and Discussion:

A total of 182 patients (30.2% men, 69.8% women) were enrolled whose mean (SD) age in years was 55 (9.0). The glycaemic status was generally poor with a prevalence of poor glycaemic control as high as 58.2%. This prevalence is higher than that previously obtained at the same hospital in 2013 thus presenting a major health challenge. This also means the burden of diabetic complications is likely to increase. Poor glycaemic control was significantly associated with gender and duration of diabetes mellitus.

Conclusion:

We conclude that in order to improve glycaemic control among diabetic patients, primary healthcare facilities need to focus on patient education and should facilitate early diagnosis through routine medical check-ups.

Keywords: Diabetes mellitus, Diabetic complications, Glycaemic control, HbA1c, WHO, Zimbabwe.

* Address correspondence to this author at the Department of Medical Laboratory Sciences, College of Health Sciences, University of Zimbabwe, P.O. Box AV 178, Avondale, Harare, Zimbabwe; Tel: +263772566214; E-mail: danaizh@live.com

1. INTRODUCTION

Diabetes mellitus is the fourth leading cause of death in most high-income countries but 80% of current cases occur in low-and-middle income countries like Zimbabwe [1]. Additionally, the International Diabetes Federation (IDF) estimated that three quarters of deaths from diabetes among people younger than 60 years of age occurred in Africa in 2013 [2, while WHO reported that the prevalence of diabetes mellitus in Zimbabwe was 4.6% in 2016, showing an increase from 0.04% reported before 1980 [3, 4]. The diabetes epidemic is accelerating in the developing world and this is likely to further increase the burden of chronic diabetic complications worldwide [5, 6].

Measurement of glycosylated haemoglobin (HbA1c) is one of the most important ways of assessing the level of glucose control and provides insight into the quality of glycaemic control over the life span of red blood cells (2-3 months) [7, 8]. HbA1c concentrations are free of daily fluctuations unlike blood glucose and show an individual's glycaemic status over a longer period hence are the best test for diabetes management [1, 9, 10]. Hence, guidelines from several prominent clinical organisations recommend that HbA1c should be measured at regular intervals in all patients with diabetes [7, 8, 11].

Good glycaemic control is defined as HbA1c less than 7% (53 mmol/mol), while HbA1c greater than or equal to 7% represents poor glycaemic control in patients with diabetes mellitus [12, 13]. There is evidence that good glycaemic control in diabetic patients can be achieved when patients are educated about the disease and become compliant [11, 14]. Hence, health care professionals should not only provide treatment but also provide lifestyle guidance and education support [15].

Patients should be educated about how compliance and glycaemic control can be affected by various factors such as socio-demographic characteristics (gender, age, weight and income), level of physical activity, dietary intake and diabetic profile (age at diagnosis, duration of diabetes, type of treatment, complication and family history) [12, 15, 16]. This study was therefore carried out to determine the extent of glucose control and factors associated with poor glycaemic control in diabetic patients attending Parirenyatwa Group of Hospitals for monitoring and treatment.

2. MATERIALS AND METHODS

2.1. Study Design

An analytical cross-sectional study involving diabetic patients attending Parirenyatwa Group of Hospitals (PGH) was carried out.

2.2. Study Period

The study was conducted from 21 December 2017 to 30 April 2018.

2.3. Participants

Diabetic patients aged 19 to 64 years, both male and female, attending the Diabetic Clinic at Parirenyatwa Group of Hospitals, who met the inclusion criteria, were enrolled in the study.

2.4. Exclusion Criteria

Diabetic patients known to have haemoglobinopathies or other erythropoietic disorders and those with documented chronic liver failure, chronic renal failure or anaemia were excluded from the study.

2.5. Sample Size

The minimum sample size required for this study was 303. This sample size was calculated using the Dobson's formula at a confidence interval of 95%, maximum tolerable error of 5% and prevalence of 27% [17].

2.6. Ethical Considerations

This study was ethically approved by the Joint Research Ethics Committee for the University of Zimbabwe, College of Health Sciences and Parirenyatwa Group of Hospitals (JREC Ref: 385/17). All information used in this study was strictly accessible to the researchers only using passwords. Samples and results were assigned laboratory identity numbers to ensure privacy, security and confidentiality.

2.7. Data and Sample Collection

Patients' demographic information (age, gender, height, weight), clinical information and EDTA blood samples were collected at Parirenyatwa Group of Hospitals Diabetic Clinic during patients' routine visits. EDTA-anticoagulated blood samples of patients who met inclusion criteria were centrifuged at 2000rpm for 5 minutes and the erythrocyte-rich deposits were aliquoted, stored in a refrigerator (2-8°C) and analysed within 7 days.

2.8. Sample Analysis

Aliquots were allowed to reach room temperature and then lysed using the HbA1c pre-treatment solution, producing a haemolysate that was used as working sample after 5 minutes. The machine was calibrated using the method provided in the supplier's manual and controls were analysed before sample analysis. Samples were analysed on the Mindray® BS 400 analyser using the International Federation of Clinical Chemists (IFCC) enzymatic method for HbA1c measurement. Test samples were run once normal and abnormal controls had produced results within their specified reference ranges to ensure accuracy of HbA1c results.

2.9. Operational Definitions

Comparisons were made with established WHO guidelines for well-managed diabetic patients. Good glycaemic control is defined as HbA1c less than 7% (53 mmol/mol), while HbA1c greater than or equal to 7% represents poor glycaemic control in patients with diabetes mellitus according to WHO reference ranges [18]. Body mass index is defined as normal (BMI < 25 kg/m^2), overweight (BMI of 25-30 kg/m^2) and obese (BMI >30 kg/m^2) [11, 19]. Hypertension is defined as a blood pressure of at least 140/90 mmHg or being on therapy for hypertension [11]. The duration of diabetes mellitus is defined as time between diagnosis and the time of recruitment into the project.

2.10. Statistical Analysis

Descriptive statistics were used to summarise the sample characteristics. Pearson's chi-squared tests and student's t-tests were used to test for associations between study variables. All data analysis was conducted using STATA® version 13.1 statistical package. All statistical tests performed were concluded at 5% level of significance.

3. RESULTS AND ANALYSIS

A total of 182 diabetic patients were enrolled in the study, 55 (30.2%) of whom were male. As shown in Table **1**, mean (SD) age in years of the diabetic patients was 55 (9.0). The study participants had median duration of diabetes mellitus of 6 (0.5-30) years.

Table 1. Summary of study population.

Patient Variable	Outcome
Age, years Mean (SD) Median (Range)	55 (9.0) 58 (25-64)
Gender Male, n (%) Female, n (%)	55 (30.2) 127 (69.8)
Duration of diabetes, years Mean (SD) Median (Range)	8.4 (7.4) 6 (0.5-30)
Blood pressure Non-hypertensive, n (%) Hypertensive, n (%)	39 (21.4) 143 (78.6)
Lipid therapy, n (%) Yes No	121 (66.5) 61 (33.5)
BMI, kg/m^2 Mean (SD) Median (Range)	26.7 (4.7) 26.2 (15.1-47.6)
HbA1c, % Mean (SD) Median (Range)	8.1 (2.4) 7.4 (4.8-15.4)

A total of 143 (78.6%) patients were hypertensive, while 121 (66.5%) of the study subjects were on lipid therapy. The mean (SD) BMI in kg/m^2 was 26.7 (4.7) while 64 (35.2%) of the diabetic patients had normal weight, 81 (44.5%) were overweight and 37 (20.3%) were obese. All the patients were non-smokers.

Of the 182 diabetic patients that took part in the study, only 76 (41.8%) had good glycaemic control (HbA1c < 7%) while the remaining 106 (58.2%) had poor glycaemic control (elevated HbA1c ≥ 7%), Table **2**.

Table 2. Test for association results between patient demographics (age, gender) and clinical profile (duration, hypertension, lipid therapy, BMI) with glycaemic control.

Variable	Good Glycaemic Control (HbA1c < 7%)	Poor Glycaemic Control (HbA1c ≥ 7%)	*P*-value
Age, years Mean (SD)	54.9 (8.4)	55.1 (9.5)	0.406
Gender Males, n (%) Females, n (%) Total, n (%)	31 (56.4) 45 (35.4) 76 (41.8)	24 (43.6) 82 (64.6) 106 (58.2)	0.007
Duration, years < 5 years, n (%) 5-9 years, n (%) 10+ years, n (%)	34 (54.8) 29 (47.5) 13 (22.0)	28 (45.2) 32 (52.5) 46 (78.0)	0.001
Blood pressure Non-hypertensive, n (%) Hypertensive, n (%)	21 (53.9) 55 (38.5)	18 (46.1) 88 (61.5)	0.062
Lipid therapy, n (%) No Yes	23 (37.7) 53 (43.8)	38 (62.3) 68 (56.2)	0.266
BMI, kg/m^2 Normal weight, n (%) Overweight, n (%) Obese, n (%)	27 (42.2) 31 (38.3) 18 (48.7)	37 (57.8) 50 (61.7) 19 (51.3)	0.561

There was no significant difference in glycaemic control according to the age of diabetic patients, p=0.406. As shown in Table **2**, the mean age was 54.9 (8.4) years for patients with good glycaemic control and 55.1 (9.5) years for patients with poor glycaemic control. However, more female patients had poor glycaemic control compared to their male counterparts (p = 0.007) (Table **2**).

There was a statistically significant difference in the duration of diabetes mellitus between the patients with good and those with poor glycaemic control, (Table **2**). Long duration of diabetes mellitus was significantly associated with poor glycaemic control (p=0.001).

Out of the 182 study participants, 78.6% were hypertensive and most of the hypertensive patients (61.5%) had poor glycaemic control as presented in Table **2**. There was no significant association between blood pressure and glycaemic control.

A total of 121 (66.5%) of the diabetic patients that participated in the study were on lipid therapy for some form of dyslipidaemia as displayed in Table **2**. Though poor glycaemic control was noted in a greater proportion (56.2%) of the participants on lipid therapy, there was no significant association between lipid therapy and glycaemic control (p=0.266). As also shown in Table **2**, there was no significant association between BMI and glycaemic control (p=0.561).

4. DISCUSSION

Diabetes is a chronic disease associated with high mortality rates due to its acute and chronic complications [1, 5, 6]. It is recommended to maintain good glycaemic control (HbA1c < 7%) in diabetic patients [20]. Apart from pharmacologic agents for glycaemic regulation, early diagnosis, treatment compliance and modifications in lifestyle are also crucial to avoid complications [5]. The prevalence of good glycaemic control in this study was lower (41.8%) when compared to a previous study at the same hospital [21]. Elevated HbA1c was found in the majority of patients (58.2%) representing poor glycaemic control in the current study. Variances in glycaemic status between the previous and this study could be due to the different reference ranges used. The previous study defined good glycaemic control as HbA1c < 9% [21] whilst this study used more stringent WHO reference ranges (HbA1c < 7%) as good control [20]. The prevalence of poor glycaemic control was higher in Ethiopia (62%), Libya (78%) and Zambia (61%) [22, 23, 24].

Poor glycaemic control is expected to become more prevalent later in life due to limited physical activity or non-adherence to treatment [22, 25]. There was, nevertheless, no significant association between age and glycaemic control in the current study (Table **2**). This agrees with findings from a previous study done in Zimbabwe [20]. Results in the present study may be owing to the fact that patients may well be physically active, hence their glucose utilisation remains high, which leads to normal blood glucose levels. In contrast, a similar Ethiopian study reported increasingly poor glycaemic control with age which became substantial above 58 years of age whereas Zambia reported high prevalence of poor glycaemic control in patients below 50 years of age [17, 23]. Many factors such as lifestyles, concurrent illnesses and socioeconomic status could play a role [11, 26].

Consistent with studies done in Oman and Scotland [14, 26], poor glycaemic control was found to be more common in female patients than in male patients in the current study (p = 0.007) (Table **2**). However, earlier studies done previously in Zimbabwe did not find a significant association between gender and glycaemic control whilst studies in India showed male predominance in terms of poor glycaemic control [20, 27]. This is possibly due to the fact that there were significantly more females than male diabetics enrolled in the current study. Furthermore, obesity and sedentary lifestyle habits are commonly reported in Zimbabwean women [18]. Increase in adipose tissue and hyperlipidaemia have been shown to cause poor glycaemic control due to the production of cytokines which ultimately result in insulin resistance [28].

Poor glycaemic control is more prevalent as the duration of diabetes mellitus increases [16]. The current study also showed that the duration of diabetes mellitus is directly related to poor glycaemic control (p = 0.001) (Table **2**).

It has been shown that the chronicity of type 2 diabetes mellitus and additional chronic illnesses can lead to dyslipidaemia and decreased β-cell function with time resulting in decreased insulin secretion and sensitivity [29]. It is also highly likely that patients with chronic diseases such as diabetes mellitus who are on long-term treatment, experience distress which together with the high cost of treatment has a negative impact on their glycaemic control.

Findings from this study revealed that glycaemic control and hypertension had no significant association between them (Table **2**). However, a high proportion of hypertensive patients had poor glycaemic control, in corroboration with other studies [27]. This could be due to the effect of some hypertensive drugs such as β-adrenoceptor antagonists and diuretics, which increase fasting blood glucose levels, through decreased insulin release [30]. Another possible explanation could be the stress and obesity associated with hypertension that result in hormonal changes which will affect blood glucose levels [11].

A greater proportion of diabetic patients who were on lipid therapy had poor glycaemic control although there was no significant association between lipid therapy and glycaemic control (Table **2**). Lipid therapy is used for the treatment of dyslipidaemia which is usually a complication of diabetes mellitus [31]. The findings of this study are similar to those from a systematic review and meta-analysis of randomized clinical trials, on the use of statins in diabetic patients, between 1966 and 2012 [32].

This study has shown that poor glycaemic control is present in a high proportion of the diabetic patients, in spite of their body mass index (Table **2**). Conflicting results were found in an Indian study, in which poor glycaemic control was associated with increased body mass index [28]. This observation could possibly be due to reduced physical activity as body mass index increases.

An increase in adipose tissue also causes impaired insulin signalling through production of pro-inflammatory cytokines such as interleukin 6 [11, 30].

CONCLUSION

Glycaemic control was generally poor with a prevalence of elevated HbA1c (poor glycaemic control) of 58.2%. Glycaemic control was not affected by age, hypertension, lipid therapy and body mass index. However, poor glycaemic control was significantly associated with female gender and longer duration of diabetes mellitus.

STRENGTHS AND LIMITATIONS OF THE STUDY

The study analysed characteristics which could be determined clinically as well as in the laboratory thus reducing bias associated with self-report. Due to its cross-sectional design, this study was able to identify associations between several factors and glycaemic control, though results could be affected by confounding by variables such as basal HbA1c. Therefore, results must be interpreted with caution. The study was also carried out at one treatment center and

results cannot be generalised to the Zimbabwean population. Other factors like adherence and type of treatment were not investigated. The minimum sample size was also not reached due to time and financial constraints. Therefore, there is a need for further comprehensive investigations.

RECOMMENDATIONS

The healthcare system should be strengthened to deliver standard care for diabetes and its complications. Effective strategies recommended to improve the current regimes at primary care level include: focus on education of diabetic patients and behavioural changes that facilitate early diagnosis through routine medical check-ups. Regular HbA1c measurements at dedicated public diabetic clinics should be done to improve glycaemic control.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was ethically approved by the Joint Research Ethics Committee for the University of Zimbabwe, College of Health Sciences and Parirenyatwa Group of Hospitals (JREC Ref: 385/17).

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all the participants prior to publication.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1]   Amod A, Ascott-Evans BH, Berg GI, Blom DJ, Brown SL, Carrihill MM, *et al.* Guideline for the management of type 2 diabetes. Journal of Endocrinology. Metabolism and Diabetes of South Africa 2012; 17(2)(Suppl. 1): S1-S95.

[2]   International Diabetes Federation. IDF Diabetes Atlas 2013. 6th Edition, https:/ /www.idf.org/ component/ attachments /attachments. html?id=813

[3]   World Health Organization. Diabetes country profiles (Zimbabwe) 2016. Available at: http:// www.who.int/ diabetes/ country -profiles/ zwe

[4]   Mutowo M, Gowda U, Mangwiro JC, Lorgelly P, Owen A, Renzaho A. Prevalence of diabetes in Zimbabwe: A systematic review with meta-analysis. Int J Public Health 2015; 60(1): 1-11.
[http://dx.doi.org/10.1007/s00038-014-0626-y] [PMID: 25432797]

[5]   Karahan F, Dede S, Ceylan E. The Effect of Lycopene Treatment on Oxidative DNA Damage of Experimental Diabetic Rats. Open Clin Biochem J 2018; 8: 1-6.
[http://dx.doi.org/10.2174/2588778501808010001]

[6]   Haigh WB, Guralski DM, Arrigo LM, *et al.* Development of a novel polyclonal antibody-based immunoassay for the quantitation of non-albumin urinary proteins. Open Clinical Chemistry Journal 2013; 6: 1-12.
[http://dx.doi.org/10.2174/1874241601306010001]

[7]   American Diabetes Association. Standards of medical care in diabetes--2012. Diabetes Care 2012; 35(1)(Suppl. 1): S11-63.
[PMID: 22187469]

[8] International Diabetes Federation, Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes. Brussels, Belgium: IDF 2005. [https://www.iapb.org/wp-content/uploads/Global-Guideline-for-Type-2-Diabetes]

[9] Sacks DB. A1C *versus* glucose testing: A comparison. Diabetes Care 2011; 34(2): 518-23. [http://dx.doi.org/10.2337/dc10-1546] [PMID: 21270207]

[10] American Diabetes Association. Standards of medical care in diabetes. The Journal of Clinical and Applied Research and Education 2017; 40(Suppl. 1).

[11] Gupta S, Jain U, Chauhan N. Laboratory diagnosis of HbA1c: A Review Journal of Nanomed Research 2017; 5(4) [http://dx.doi.org/10.15406/jnmr.2017.05.00120]

[12] Mansour AA, Said S, Zainuddin H. Predictors of poor glycaemic control among type 2 diabetic patients. Afr J Med Med Sci 2013; 3(2)

[13] Rayman G. Glycaemic control, glucose variability and the Triangle of Diabetes Care British Journal of Diabetes 2016; 16 (Supplement 1)

[14] Venugopal S, Kunju R, Al Harthy S, Al Zadjali N. Hemoglobin A1c in Muscat, Oman - A 3 year study. Oman Med J 2008; 23(3): 170-2. [PMID: 22359708]

[15] Camara A, Baldé MN, Sobngwi-Tambekou J, Kengne AP, Diallo MM, Tchatchoua APK, *et al.* Poor glycaemic control in type 2 diabetes in the South of the Sahara; the issue of limited access to an HbA1c test. Diabetes Research and Clinical Practice, Elsevier 2014; 108(1)

[16] Viana LV, Leitão CB, Kramer CK, *et al.* Poor glycaemic control in Brazilian patients with type 2 diabetes attending the public healthcare system: A cross-sectional study. BMJ Open 2013; 3(9): e003336. [http://dx.doi.org/10.1136/bmjopen-2013-003336] [PMID: 24052610]

[17] Ismail A, Suddin LS, Sulong S, Ahmed Z, Kamaruddin NA, Sukor N. Profiles and factors associated with poor glycemic control among inpatients with diabetes mellitus type 2 as a primary diagnosis in a teaching hospital. Indian J Community Med 2016; 41(3): 208-12. [http://dx.doi.org/10.4103/0970-0218.183590] [PMID: 27385874]

[18] National survey, 2005: Zimbabwe Non-Communicable disease Risk factors-ZiNCoDs Preliminary report. Available at: http://ghdx.healthdata. org/ record/ zimbabwe-steps -noncommunicable -disease -risk -factors- survey -2005

[19] Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: Epidemiology and public health implications. A systematic review. BMC Public Health 2011; 11: 564. [http://dx.doi.org/10.1186/1471-2458-11-564] [PMID: 21756350]

[20] Chako KZ, Phillipo H, Mafuratidze E, Zhou DT. Significant differences in the prevalence of elevated HbA1c levels for type I and Type II diabetics attending the parirenyatwa diabetic clinic in Harare, Zimbabwe. Chinese Journal of Biology 2014. Article ID 672980, 5 pages

[21] Clinical Practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes 2008; 32(Suppl. 1): 1-215.

[22] Fseha B. Glycaemic control and its associated factors in type 2 diabetic patients in suhul hospital, Northwest Tigray, Ethiopia. J Diabetes Metab 2017; 8(3): 729. [http://dx.doi.org/10.4172/2155-6156.1000729]

[23] Ashur ST, Shah SA, Bosseri S, Fah TS, Shamsuddin K. Glycaemic control status among type 2 diabetic patients and the role of their diabetes coping behaviours: A clinic-based study in Tripoli, Libya. Libyan J Med 2016; 11(1): 31086. [http://dx.doi.org/10.3402/ljm.v11.31086] [PMID: 28349838]

[24] Musenge EM, Michelo C, Mudenda B, Manankov A. Glycaemic control and associated self-management behaviours in diabetic outpatients: A hospital based observation study in Lusaka, Zambia. J Diabetes Res 2016; 2016: 7934654. [http://dx.doi.org/10.1155/2016/7934654] [PMID: 26798654]

[25] Aronson R, Orzech N, Ye C, Brown RE, Goldenberg R, Brown V. Specialist-led diabetes registries and prevalence of poor glycemic control in type 2 diabetes: The diabetes registry outcomes project for A1C reduction (DROP A1C). Diabetes Care 2016; 39(10): 1711-7. [http://dx.doi.org/10.2337/dc15-2666] [PMID: 27515966]

[26] Collier A, Ghosh S, Hair M, Waugh N. Impact of socioeconomic status and gender on glycaemic control, cardiovascular risk factors and diabetes complications in type 1 and 2 diabetes: A population based analysis from a Scottish region. Diabetes Metab 2015; 41(2): 145-51. [http://dx.doi.org/10.1016/j.diabet.2014.09.004] [PMID: 25454092]

[27] Khattab M, Khader YS, Al-Khawaldeh A, Ajlouni K. Factors associated with poor glycemic control among patients with type 2 diabetes. J Diabetes Complications 2010; 24(2): 84-9. [http://dx.doi.org/10.1016/j.jdiacomp.2008.12.008] [PMID: 19282203]

[28] Makki K, Froguel P, Wolowczuk I. Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. ISRN Inflamm 2013; 2013: 139239. [http://dx.doi.org/10.1155/2013/139239] [PMID: 24455420]

[29] Hirst JA, Farmer AJ, Feakins BG, Aronson JK, Stevens RJ. Quantifying the effects of diuretics and β-adrenoceptor blockers on glycaemic control in diabetes mellitus - A systematic review and meta-analysis. Br J Clin Pharmacol 2015; 79(5): 733-43. [http://dx.doi.org/10.1111/bcp.12543] [PMID: 25377481]

[30] Ozougwu JC, Obimba KC, Belonwu CD, Unakalamba CB. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. Journal of Physiology and Pathophysiology 2013; 4(4): 46-57. [http://dx.doi.org/10.5897/JPAP2013.0001]

[31]   Schofield JD, Liu Y, Rao-Balakrishna P, Malik RA, Soran H. Diabetes Dyslipidemia. Diabetes Ther 2016; 7(2): 203-19.
[http://dx.doi.org/10.1007/s13300-016-0167-x] [PMID: 27056202]

[32]   Zhou Y, Yang Yuan Y, Cai R-R, *et al*. Statin therapy on glycaemic control in type 2 diabetes: A meta-analysis, Expert Opinion on Pharmacotherapy, 14:12, 1575-1584
[http://dx.doi.org/10.1517/14656566.2013]