Addition of Insulin to Treatment Regimen in Type 2 Diabetes: The Significance of Age and Duration among Sudanese Diabetic Patients

Hisham Mohammed Abdelrahim1, Abdelhaleem Mustafa Madani2,3, Asma Noureldaim Mahmoud4, Tarig Mohammed El-hadiyah1, Abubakr Khidir Yousif5

1Medicine and Endocrinology, University of National Ribat, Khartoum, Sudan
2Clinical Pharmacy, Pharmacology Department, Faculty of Pharmacy, International University of Africa, Khartoum, Sudan
3Cardiac Center, Omdurman Teaching Hospital, Omdurman, Sudan
4Department of Pharmacy Practice, Faculty of Pharmacy, International University of Africa, Khartoum, Sudan
5Consultant of Pharmaceutical Microbiology, Health Services Directorate, National Health Insurance Fund, Wadmadani, Gezira State, Sudan

Email: abubarkhidir@hotmail.com

Abstract

Background: Type 2 diabetes is a progressive disease and as the result of patient’s age and diabetes duration, β-cell ability for insulin secretion deteriorates continually and finally fails to meet body requirement. Intensification of treatment drug regimen including addition of insulin is critical to maintain glycemic target and reduce developing of long-term complications.

Objective: The main purpose of this study was to investigate the effect of diabetes duration and patients’ age on addition of insulin to treatment regimen.

Methods: A single centre, cross-sectional hospital-based study was done among 351 diabetes Mellitus (DM) patients visiting Ribat University Hospital Diabetic Clinic, Khartoum State, Sudan. Data was collected using constructed, validated and multiple-choice questionnaire. Results: From 351 patients enrolled in the study, female were 65.8% and male 34.2%. About 64.4% were on oral anti-diabetic; 35.6% on insulin; about 31.6% shifted to insulin when their ages above 40 years; and 22.8% when diabetes duration was above 5 years. Co-morbidity was 54.4% and 60.2% of patients had hypertension.

Conclusion: Interactions between age and longer duration of diabetes were mostly significant reasons for transferring patients to insulin. Percent of insulin users and co-morbidity was within international range.

Keywords

Type 2 Diabetes, Insulin, Duration, Age, Sudanese
1. Introduction

Diabetes control is complicated [1] and required continuous assessment from both patients and their specialized medical providers [2]. Although diabetes self-management skills for the Type 2 DM patient are improved with longer disease duration, the challenge to keep the required goal for diabetes control becomes harder. Resistance to medications or abnormalities of insulin production may occur and therefore increasing doses, or additional medications, or even changing treatment plan may be needed over time. This resistance is attributed to the fact that β-cell function deteriorates with time due to lipotoxicity or glucotoxicity [3]. Many studies, including United Kingdom Prospective for Diabetes Study (UKPDS) [4], proved the reduction of beta-cell function is associated to duration of diabetes [4] [5] [6] [7] [8] that requiring intensification of oral therapy, including addition of insulin to treatment regimen, considering patient-centered approach [9].

The incident of diabetes increases with age [10] and according to 2005-2006, the National Health and Nutrition Examination Survey in USA, one third of elderly population were diabetes [11]. There are many reasons related to increased incidence of diabetes among elderly, however the important one is that the β cell proliferative capacity reduced, and in diabetic individuals this effect further aggravated by higher rates of β-cell apoptosis [12]. Several studies revealed that age and diabetes duration are independent predictors for co-morbidity even hyperglycemia does not existed [13] [14]. Due to the progressive decline of β-cell function related to diabetes duration old aging, insulin therapy is more suitable choice in such patients’ population with type 2 diabetes if risk of hypoglycemia properly monitored [15].

Studies that discuss the factors associated with diabetes’ poor control and importance of intensification of drug treatment are rare and scattered, so carrying out of this study will contribute to effort that improves pharmaceutical patient care and also availability of data that push research in Sudan forward.

2. Material and Methods

2.1. Patients Characteristics

A cross-sectional study was carried out during six month from August 2012 to February 2013. From 398 patients attending to Ribat University Hospital Diabetic Clinic (RUHDC), 351 type 2 diabetes were recruited in this study.

2.2. Inclusion and Exclusion Criteria

All type 2 DM non-pregnant patients taking medications for 3 months or more were included in this study.

2.3. Instrument of Data Collection

Multiple-choice questionnaire constructed from recent literature and validated by Ribat University staff members who are expert in diabetes management. Pilot
study carried out through random distribution of ten questionnaire copies to pa-
tients who informed first about purpose of this study. After minor changes in
questionnaire content, data directly and verbally taken from patients, whilst pa-
tients’ cards also used to obtain some patients data.

2.4. Assessment of Significant of Age and Duration of Diabetes on
Addition of Insulin

Information including socio-demographic characteristic, diabetes co-morbidity,
diabetes duration, patients’ life style (exercise and diet program) and medication
adherence were obtain from all patients. Poor controlled patients who shifted to
regimen containing insulin asked about their life style, medication adherence,
before they shifted to insulin, and their ages and diabetes duration at that time
were specifically stated.

2.5. Data Analysis

Data were analyzed, using social package for social science (SPSS) version 16, to
assess patient’s answers. Descriptive and chi-square statistics were used. The dif-
fferences considered significant at p ≤ 0.05.

3. Results

From 351 patients seen in the study female were 65.8% and male 34.2%. Patients’
ages above 60 years were 48.4% and 44.16% had basic education level (Table 1).
About 64.4% were on oral anti-diabetic, 35.6% on insulin (Table 2). About
31.6% shifted to insulin when their ages above 40 years and 22.8% when diabetes
duration was above 5 years. Only 7.4% and 5.7% of insulin users had exercise
and diet program respectively (Table 2). Co-morbidity was 54.4% and 26.4% of
patients with co-morbidity their ages were above 60 years, while 13.9% their di-
abetes duration was more than 5 years (Table 3). Hypertension (60.2%) was the
major cause of co-morbidity (Table 4).

4. Discussion

Many factors are associated with diabetes poor control including old age, obesi-
ty, socio-demographic and economic status, sedentary life style, long duration of
diabetes, eating unhealthy food and poor medications adherence. In this study
the most two significant factors associated with transferring patients to insulin
were advancing age (p < 0.001) and duration of diabetes (p = 0.012). As guide-
line in RUHDC patients considered poor controlled if oral treatment intensifica-
tion failed and A1C target is sustained to be more than 8% then the patient should
shifted to treatment regimen consist of insulin.

Intensification of treatment in type 2 diabetes, including addition of insulin to
achieve target goals and to avoid long-term complications, is recommended by
many research leaders such as UKPDS [4] and American diabetes association
[16]. More than one fifth (22.8%) of our patients shifted to insulin when their
Table 1. Sociodemographic Characteristics.

| Variable   | Frequency | Percent |
|------------|-----------|---------|
| Gender     |           |         |
| Male       | 120       | 34.2    |
| Female     | 231       | 65.8    |
| Age        |           |         |
| 20 - 40    | 86        | 24.5    |
| 41 - 60    | 95        | 27.1    |
| Above 60   | 170       | 48.4    |
| Educational level |     |         |
| Basic      | 155       | 44.16   |
| Illiterate | 74        | 21.08   |
| High secondary | 59 | 16.81  |
| University | 49        | 13.96   |
| Non-formal | 14        | 3.99    |

Table 2. Significance of many variables on transferring patients to insulin regimen.

| Variables      | Insulin users N (%) | Oral anti-diabetic N (%) | p value |
|----------------|---------------------|--------------------------|---------|
| Gender         | 125 (35.6)          | 226 (64.4)               |         |
| Female         | 74 (21.1)           | 69 (19.7)                | 0.035   |
| Male           | 51 (14.5)           | 157 (44.7)               |         |
| Age (years)    |                     |                          | < 0.001*|
| 20 - 40        | 14 (4.0)            | 72 (20.5)                |         |
| 41 - 60        | 70 (19.9)           | 25 (7.1)                 |         |
| Above 60       | 41 (11.7)           | 129 (36.8)               |         |
| Duration (years)|                     |                          | 0.012*  |
| ≤5             | 45 (12.8)           | 114 (32.5)               |         |
| 6 - 10         | 36 (10.3)           | 62 (17.7)                |         |
| Above 10       | 44 (12.5)           | 50 (14.2)                |         |
| Exercise program|                     |                          | 0.434   |
| Yes            | 26 (7.4)            | 44 (12.5)                |         |
| No             | 99 (28.2)           | 182 (51.9)               |         |
| Diet program   |                     |                          | 0.376   |
| Yes            | 20 (5.7)            | 32 (9.1)                 |         |
| No             | 105 (29.9)          | 194 (55.3)               |         |
| Medication adherence |     |                          | 0.479   |
| Adherent       | 57 (16.2)           | 100 (28.5)               |         |
| Non adherent   | 68 (19.4)           | 126 (35.9)               |         |

*Consider being significant < 0.05.
duration of diabetes was more than five years to protect the patient from long term complication.

Majority of our patients shifted to insulin at age above 40 (mainly 41 - 60) and this consistent with fact that beta cell function decline with age progression [10] [15] [17].

In this study, co-morbidity was slightly more than one half and this result is low than reported by Al Hayek and his colleagues from Saudi Arabia who reported 60.9% had one complication affected the general health [18]. Co-morbidity in our study, although insignificant, was high among patients above 60 years and patients their duration more than 5 years and this consistent with many studies [10] [12] [13] [15] [17].

Several studies [19] [20] [21] revealed hypertension is common co-morbidity among patients with diabetes. A systemic literature review revealed that hypertension rates in most studies presented rates above 50%, and many presented rates above 75% [22]. The prevalence of hypertension in this work was 60.7% and this less than Waly study [19] from Egypt who reported 68%. In contrast our result is high than Al Slail [23] and Almetwazi [24] studies from Saudi Arabia reported 45% and 54.53% respectively.
Although there is marked reduction in risk of eye diseases among patients of diabetes over the last 30 years from 90% to less than 50% still it is great problem [25]. Almost 10% of our patients told they had eye diseases and this consisted within that found in literature such as a systemic review reported by Ruta and his colleagues who stated 27.9% as prevalence of diabetes [26].

Only 1% of our patients had kidney diseases and this result is low than that reported Al-Rubeaan [27] study from Saudi Arabia showed 10.8 % and Farahat study [28] from Egypt reported macro-albuminuria was 12.8% among type 2 diabetic patients.

5. Conclusion

Many factors are included in transferring type 2 DM patients; however, interactions between age and longer duration of diabetes were abundant. Percent of diabetes co-morbidity was within international range. With regard to nephropathy and retinopathy, our patients required further more thorough screening.

6. Limitation

Although RUHDC is one of the largest centers in Sudan, conducting this study in single centre will not give the complete picture about effect of diabetes duration and patients' age on treatment intensification among type 2 DM in Sudan as a whole, so generalized study funded by considerable organization or research institute is urgently recommended.

Acknowledgements

This research is a part of project presented to RUHDC after approval of the study proposal at faculty of postgraduate studies at Ribat University. The project started in 2012 and extended to 2017. The authors funded the project from their self-resources in collaborative manner. We would like to express our deep thank to the RUHDC; workers and doctors for their fine dealing during the period of data collection. Gratefulness to my patients; who allow me to interview them, despite suffering from pain of the disease and life pressures, they gave me their fruitful of their experience.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Juarez, D.T., et al. (2012) Peer Reviewed: Factors Associated With Poor Glycemic Control or Wide Glycemic Variability among Diabetes Patients in Hawaii, 2006-2009. Preventing Chronic Disease, 9, Article No. 120065.
https://doi.org/10.5888/pcd9.120065

[2] Jarvis, J., Skinner, T.C., Carey, M.E. and Davies, M.J. (2010) How Can Structured Self-Management Patient Education Improve Outcomes in People with Type 2 Di-
12. Older Adults: Standards of Medical Care in Diabetes—2019. Diabetes Care, 42, S139-S147. https://doi.org/10.2337/dc19-S012

10. Kushner, J.A. (2013) The Role of Aging upon β Cell Turnover. The Journal of Clinical Investigation, 123, 990-995. https://doi.org/10.1172/JCI64095

11. Cowie, C.C., et al. (2009) Full Accounting of Diabetes and Pre-Diabetes in the US Population in 1988-1994 and 2005-2006. Diabetes Care, 32, 287-294. https://doi.org/10.2337/dc08-1296

12. Johnson, J.D., Yang, Y.H.C. and Luciani, D.S. (2013) Mechanisms of Pancreatic β-Cell Apoptosis in Diabetes and Its Therapies. In: Islam, M., Ed., Islets of Langhans, 2nd Edition, Springer, Dordrecht, 1-20. https://doi.org/10.1007/978-94-007-6884-0_14-2

13. Zoungas, S., et al. (2014) Impact of Age, Age at Diagnosis and Duration of Diabetes on the Risk of Macrovascular and Microvascular Complications and Death in Type 2 Diabetes. Diabetologia, 57, 2465-2474. https://doi.org/10.1007/s00125-014-3369-7

14. Huang, E.S., et al. (2014) Rates of Complications and Mortality in Older Patients with Diabetes Mellitus: The Diabetes and Aging Study. JAMA Internal Medicine, 174, 251-258.

15. Kim, K.S., et al. (2012) Management of Type 2 Diabetes Mellitus in Older Adults. Diabetes & Metabolism Journal, 36, 336-344. https://doi.org/10.4093/dmj.2012.36.5.336

16. American Diabetes Association (2019) Glycemic Targets: Standards of Medical Care in Diabetes—2019. Diabetes Care, 42, S61-S70. https://doi.org/10.2337/dc19-S006

17. Gunasekaran, U. and Gannon, M. (2011) Type 2 Diabetes and the Aging Pancreatic Beta Cell. Aging, 3, 565-575. https://doi.org/10.18632/aging.100350

18. Al Hayek, A.A., et al. (2014) Factors Associated with Health-Related Quality of Life among Saudi Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Survey. Diabets, Obesity and Metabolism, 12, 12-19. https://doi.org/10.1111/j.1463-1326.2009.01098.x

[3] Arunachalam, S., Pichiah, P.T. and Achiraman, S. (2013) Doxorubicin Treatment Inhibits PPARγ and May Induce Lipotoxicity by Mimicking a Type 2 Diabetes-Like Condition in Rodent Models. FEBs Letters, 587, 105-110. https://doi.org/10.1016/j.fels.2012.11.019

[4] UK Prospective Diabetes Study Group (1995) Prospective Diabetes Study 16: Overview of 6 Years’ Therapy of Type II Diabetes: A Progressive Disease. Diabetes, 44, 1249-1258. https://doi.org/10.2337/diab.44.11.1249

[5] Bagust, A. and Beale, S. (2003) Deteriorating Beta-Cell Function in Type 2 Diabetes: A Long-Term Model. QJM: An International Journal of Medicine, 96, 281-288. https://doi.org/10.1093/qjmed/hcg040

[6] Zangeneh, F., et al. (2006) Effects of Duration of Type 2 Diabetes Mellitus on Insulin Secretion. Endocrine Practice, 12, 388-393. https://doi.org/10.1016/j.epr.2012.04.388

[7] Verma, M., Paneri, S., Badi, P. and Raman, P.G. (2006) Effect of Increasing Duration of Diabetes Mellitus Type 2 on Glycated Hemoglobin and Insulin Sensitivity. Indian Journal of Clinical Biochemistry, 21, 142. https://doi.org/10.1007/BF02913083

[8] Turner, R.C., Cull, C.A., Frighi, V. and Holman, R.R. (1999) Glycemic Control with Diet, Sulfonylurea, Metformin, or Insulin in Patients with Type 2 Diabetes Mellitus: Progressive Requirement for Multiple Therapies (UKPDS 49). The Journal of the American Medical Association, 281, 2005-2012.

[9] Association, A.D. (2019) 12. Older Adults: Standards of Medical Care in Diabetes—2019. Diabetes Care, 42, S139-S147. https://doi.org/10.2337/dc19-S012

[10] Kushner, J.A. (2013) The Role of Aging upon β Cell Turnover. The Journal of Clinical Investigation, 123, 990-995. https://doi.org/10.1172/JCI64095

[11] Cowie, C.C., et al. (2009) Full Accounting of Diabetes and Pre-Diabetes in the US Population in 1988-1994 and 2005-2006. Diabetes Care, 32, 287-294. https://doi.org/10.2337/dc08-1296

[12] Johnson, J.D., Yang, Y.H.C. and Luciani, D.S. (2013) Mechanisms of Pancreatic β-Cell Apoptosis in Diabetes and Its Therapies. In: Islam, M., Ed., Islets of Langhans, 2nd Edition, Springer, Dordrecht, 1-20. https://doi.org/10.1007/978-94-007-6884-0_14-2

[13] Zoungas, S., et al. (2014) Impact of Age, Age at Diagnosis and Duration of Diabetes on the Risk of Macrovascular and Microvascular Complications and Death in Type 2 Diabetes. Diabetologia, 57, 2465-2474. https://doi.org/10.1007/s00125-014-3369-7

[14] Huang, E.S., et al. (2014) Rates of Complications and Mortality in Older Patients with Diabetes Mellitus: The Diabetes and Aging Study. JAMA Internal Medicine, 174, 251-258.

[15] Kim, K.S., et al. (2012) Management of Type 2 Diabetes Mellitus in Older Adults. Diabetes & Metabolism Journal, 36, 336-344. https://doi.org/10.4093/dmj.2012.36.5.336

[16] American Diabetes Association (2019) Glycemic Targets: Standards of Medical Care in Diabetes—2019. Diabetes Care, 42, S61-S70. https://doi.org/10.2337/dc19-S006

[17] Gunasekaran, U. and Gannon, M. (2011) Type 2 Diabetes and the Aging Pancreatic Beta Cell. Aging, 3, 565-575. https://doi.org/10.18632/aging.100350

[18] Al Hayek, A.A., et al. (2014) Factors Associated with Health-Related Quality of Life among Saudi Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Survey. Diabetes, Obesity and Metabolism, 12, 12-19. https://doi.org/10.1111/j.1463-1326.2009.01098.x
abetes & Metabolism Journal, 38, 220-229.  
https://doi.org/10.4093/dmj.2014.38.3.220

[19] Waly, E.H. and Hamed, M.S. (2018) Hypertension and Dyslipidemia among Type II Diabetic Patients and Related Risk Factors and Complications. Egyptian Journal of Community Medicine, 36, 31-43. https://doi.org/10.21608/ejcm.2018.6868

[20] Gadallah, M., Abdel Megid, S., Mohsen, A. and Kandil, S. (2018) Hypertension and Associated Cardiovascular Risk Factors among Urban Slum Dwellers in Egypt: A Population-Based Survey. Eastern Mediterranean Health Journal, 24, 435-442. https://doi.org/10.26719/2018.24.5.435

[21] Unadike, B., Erege, A. and Ohwovoriole, A. (2011) Prevalence of Hypertension amongst Persons with Diabetes Mellitus in Benin City, Nigeria. Nigerian Journal of Clinical Practice, 14, 300-302. https://doi.org/10.4103/1119-3077.86772

[22] Colosia, A.D., Palencia, R. and Khan, S. (2013) Prevalence of Hypertension and Obesity in Patients with Type 2 Diabetes Mellitus in Observational Studies: A Systematic Literature Review. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 6, 327-338. https://doi.org/10.2147/DMSO.S51325

[23] Al Slail, F.Y., Abid, O., Assiri, A.M., Memish, Z.A. and Ali, M.K. (2016) Cardiovascular Risk Profiles of Adults with Type-2 Diabetes Treated at Urban Hospitals in Riyadh, Saudi Arabia. Journal of Epidemiology and Global Health, 6, 29-36. https://doi.org/10.1016/j.jegh.2015.07.004

[24] Almetwazi, M., et al. (2019) Factors Associated with Glycemic Control in Type 2 Diabetic Patients in Saudi Arabia. Saudi Pharmaceutical Journal, 27, 384-388. https://doi.org/10.1016/j.jsps.2018.12.007

[25] Antonetti, D.A., Klein, R. and Gardner, T.W. (2012) Diabetic Retinopathy. New England Journal of Medicine, 366, 1227-1239. https://doi.org/10.1056/NEJMra1005073

[26] Ruta, L., et al. (2013) Prevalence of Diabetic Retinopathy in Type 2 Diabetes in Developing and Developed Countries. Diabetic Medicine, 30, 387-398. https://doi.org/10.1111/dme.12119

[27] Al-Rubeaan, K., et al. (2014) Diabetic Nephropathy and Its Risk Factors in a Society with a Type 2 Diabetes Epidemic: A Saudi National Diabetes Registry-Based Study. PLoS ONE, 9, e88956. https://doi.org/10.1371/journal.pone.0088956

[28] Farahat, T.M., Kamal Elsaed, G., Sayed Gazareen, S. and Ibrahim Elsayed, T. (2014) Prevalence of Proteinuria among Type 2 Diabetic Patients in Menoufia Governorate, Egypt. Menoufia Medical Journal, 27, 363-371. https://doi.org/10.4103/1110-2098.141710