Review Article:

Factors associated with poor control of type 2 diabetes mellitus: A systematic review and Meta-analysis

* T.S. Sanal[1], N. S. Nair[2], P. Adhikari[3]

Abstract:

Diabetes is estimated to be responsible for 3.96 million adult deaths per year at global level. By 2025, the number of people with diabetes in India is estimated to rise to 70 million. In spite of well-defined treatment for type 2 diabetes, in majority of the people, disease is poorly controlled. Hence controlling the disease is a major issue to prevent complications, increase the life expectancy and improve the quality of life. To find out the factors associated with poor control of diabetes, a systematic review and meta-analysis was carried out. The data source was Published and unpublished studies from 1980 to October 2010. Two of the authors applied selection criteria to get the relevant studies. Glycated hemoglobin level was the measure for outcome. Meta-analysis was performed by pooling the results of selected studies. Mantel – Haenszel Odds Ratios, standardized mean differences and 95 % Confidence Intervals of estimates were calculated for Meta-analysis. The results were presented using forest plot. Meta-analysis showed that, elderly people and males had better control on diabetes. Presence of coronary heart disease and non-adherence to diet, exercise, medication and glucose monitoring are the factors associated with poor control of diabetes. Neuropathy, retinopathy, renal failure and neurological disorders are the complications of poor control. In spite of our sincere attempt to consolidate all studies, which give evidence of factors responsible for poor control of diabetes, we did not find this as the primary objective in many well-conducted studies. Hence, this area requires more attention of diabetes researchers.

Key words: Health care management, Poor control of diabetes, Meta-analysis

Introduction:

Diabetes mellitus is one of the most common chronic diseases, among adults. Globally, the number of adults with diabetes in 2010 was estimated to be 285 million, with prevalence of 6.4 %. By 2030, the estimated number will increase to 439 million with prevalence of 7.7 % (1). Number of deaths in adult due to diabetes is estimated to be 3.96 million per year and mortality rate of diabetes in all ages is 6.8 %, at global level (2).

[1]T.A Pai Management Institute (TAPMI), Manipal, Karnataka, India

[2]Department of Statistics, Manipal University,

Manipal, Karnataka, India

[3]Kasturba Medical College (K.M.C) Hospital,

Attavar, Mangalore, Karnataka, India

***Corresponding Author:**
Sanal TS
Faculty Associate
T.A Pai Management Institute (TAPMI), Manipal, Karnataka, India

E-mail: sanal.statistics@gmail.com

In India, currently, there are 40 million people with diabetes. By 2025 this number is estimated to rise to 70 million. This means that every fifth diabetic in the world would be an Indian (3). Type 2 diabetes is also a growing cause of disability and premature death, mainly due to cardiovascular disease and other chronic complications (4). Lifestyle and nutritional status etc influence the prevalence of glucose intolerance and complications of diabetes (5).

Prevention, early identification and systematic follow up of treatment are the basic strategies for controlling the disease. In spite of well-defined treatment for type 2 diabetes, in majority of the people, disease is poorly controlled with existing therapies (6-7). Hence it would be interesting to identify the factors associated with poor control of diabetes. There are number of studies which have attempted to address this question. However, as far as our knowledge is concerned, no attempt has been made to consolidate the data in the form of a systematic review. Hence, we carried out this systematic review.

Method

Study eligibility

All studies conducted on people with type 2 diabetes from 1980 to October 2010 irrespective of region or languages were included. This includes case control, cohort and cross-sectional studies which made an attempt to address the factors, responsible for poor control of diabetes. The studies conducted on people with type 1 and gestational diabetes was excluded. Glycated hemoglobin level (HbA1c) was the measure for outcome with two categories. HbA1C > 7 % is considered as poor control and Hb1c < 7 % as good control (8).

Search strategy

A comprehensive search was done by using the keywords, "causes of uncontrolled AND type 2 diabetes", "factors of poor control AND type 2 diabetes", "factors of uncontrolled AND type 2 diabetes", "poor control AND type 2 diabetes" and "uncontrolled AND type 2 diabetes".

The journals and databases used are Diabetes (1980 to 2010), Diabetes Care (1980 to 2010), Diabetes Educator (1980 to 2010), Diabetes and Metabolism (1990 to 2010), International Journal of Diabetes in Developing Countries (2001 to June 2010), Indian Journal of Medical Research (2003 to march 2010), Journal of Diabetology (2010), New England Journal of Medicine (1980 to 2010), Public Library of Science and Pub Med (1980 to October 2010). References of the included studies were also searched further.

Selection of studies

A two-phase strategy was adopted for selection of studies. In the first phase, titles and abstracts obtained with preliminary search were scrutinized for inclusion. In the second phase, full manuscripts of all the studies qualified in phase one, were obtained. Selection criteria were applied to each of these studies by two of the authors. Valid studies were included for final data extraction, based on pre-designed proforma.

Quality assessment

Methodological quality of the selected studies was assessed with the help of Critical Appraisal of Evidence Effectiveness tool (case- control). This tool has been endorsed by the Joanna Briggs Institute (JBI) (9). Internal consistency was tested, using Cronbach alpha and it was found to be 0.728.

Data synthesis

From the selected studies, patient, treatment and disease related factors of diabetes were extracted. For Meta-analysis, Odds Ratio (O.R.) with 95 % Confidence Interval (C.I.) and mean with Standard Deviation (S.D.) were retrieved. If O.R. and C.I were not reported, those measures were calculated from the available data. O.R.s of the selected studies was combined and Mantel- Haenszel Odds Ratio (M.H. O.R.) was calculated with poor control of diabetes as reference. For continuous variables standardized mean difference with 95 % C.I. was also calculated. The results were presented using forest plot with fixed effect model. Chi- square statistics with P value < 0.10 and I2 statistics > 65% were used to test the heterogeneity, among the selected studies (10). Meta-analysis was performed using the Review Manager Software (Rev Man 5) from the Cochrane library (11).

Results

Over all 7,501 studies were identified from the initial search, of which 7,458 studies were excluded and 43 studies were retrieved, in phase one. Out of this, 22 studies were excluded from the review because of either not having satisfactory inclusion criteria or insufficient information. Remaining 21 studies were included in the review of which 10 studies qualified for Meta-analysis in phase two. (figure.1)

Patient related factors

Age, gender, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), smoking, depression, level of knowledge on diabetes, calcium channel blockers, acetyl salicylic acid and creatinine were included in patient related factors. Control of diabetes was poor among younger adults (< 60 years) compared to elders (M.H. O.R. = 1.61, 95 % C.I. = 1.11 to 2.33). Males (M.H. O.R. = 0.80, 95 % C.I. = 0.72 to 0.88) had better diabetes control compared to females. Habit of smoking (M.H. O.R. = 0.89, 95 % C.I. = 0.75 to 1.06) and presence of depression (M.H. O.R. = 0.93, 95 % C.I. = 0.69 to 1.26) had no association with poor control. There was a difference in mean BMI of poorly controlled and well controlled diabetics (standardized mean difference is 0.47 with 95 % C.I. is 0.38 to 0.55). Increase in SBP and DBP was not associated with poor control of diabetes. Meta-analysis results of patient related factors are shown in figure 2 and table 1.

Figure 1. Flow chart of the selection of studies

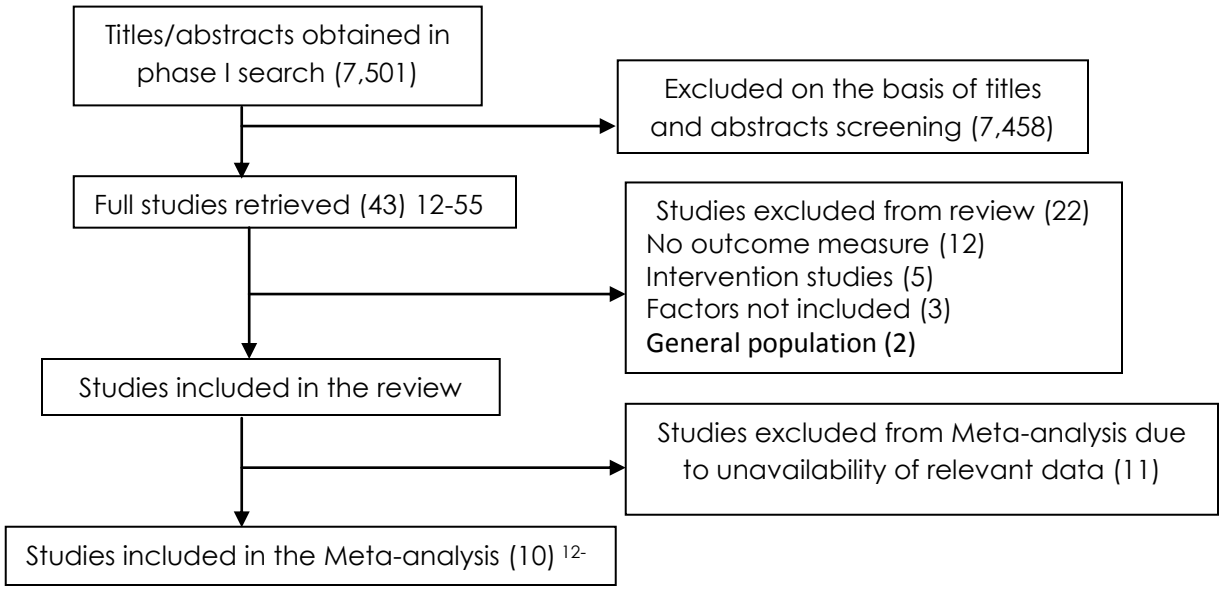


Table 1. Patient related factors (Continuous variables)

Study	Poor control		Control		Standardized Mean difference, Fixed, 95 % C.I.
	No	Mean (S.D.)	No	Mean (S.D.)	
BMI					
Bash 2008	694	31.5 (8.6)	1177	27.7 (6.1)	0.53 (0.44 to 0.63)
Curtiss 2001	123	33.6 (7.4)	324	31.9 (7.5)	0.23 (0.02 to 0.44)
Demirtunc 2009	35	29.9 (5.5)	35	29.3 (3.7)	0.13 (-0.34 to 0.60)
Total	852		1536		0.47 (0.38 to 0.55)
Test for heterogeneity: χ^2 = 8.95, P = 0.01, I^2 = 78 %					
Test for overall effect: Z = 10.76, P = < 0.001					
SBP					
Bash 2008	694	128 (47.2)	1177	128 (19.3)	0.00 (-0.09 to 0.09)
Curtiss 2001	123	130 (18.0)	324	130 (18.0)	0.01 (-0.20 to 0.21)
Demirtunc 2009	35	146 (21.0)	35	139 (19.0)	0.35 (-0.13 to 0.82)
Total	852		1536		0.01 (-0.17 to 0.10)
Test for heterogeneity: χ^2 = 1.98, P = 0.37, I^2 = 0 %					
Test for overall effect: Z = 0.28, P = 0.78					
DBP					
Bash 2008	694	72 (26.5)	1177	74 (10.7)	-0.09 (-0.19 to 0.00)
Curtiss 2001	123	79 (10.0)	324	78 (10.0)	0.10 (-0.11 to 0.31)
Demirtunc 2009	35	87 (15.0)	35	81 (11.0)	0.45 (-0.02 to 0.93)
Total	852		1536		-0.04 (-0.13 to 0.04)
Test for heterogeneity: χ^2 = 7.08, P = 0.03, I^2 = 72 %					
Test for overall effect: Z = 1.03, P = 0.73					
Creatinine					
Bash 2008	694	0.9 (0.5)	1177	0.9 (0.2)	0.00 (-0.09 to 0.09)
Curtiss 2001	35	0.7 (0.2)	35	0.8 (0.2)	-0.44 (-0.91 to 0.04)
Total	729		1212		-0.02 (-0.11 to 0.08)
Test for heterogeneity: χ^2 = 3.16, P = 0.08, I^2 = 68 %					
Test for overall effect: Z = 0.35, P = 0.73					

Figure 2. Patient related factors (Categorical variables)

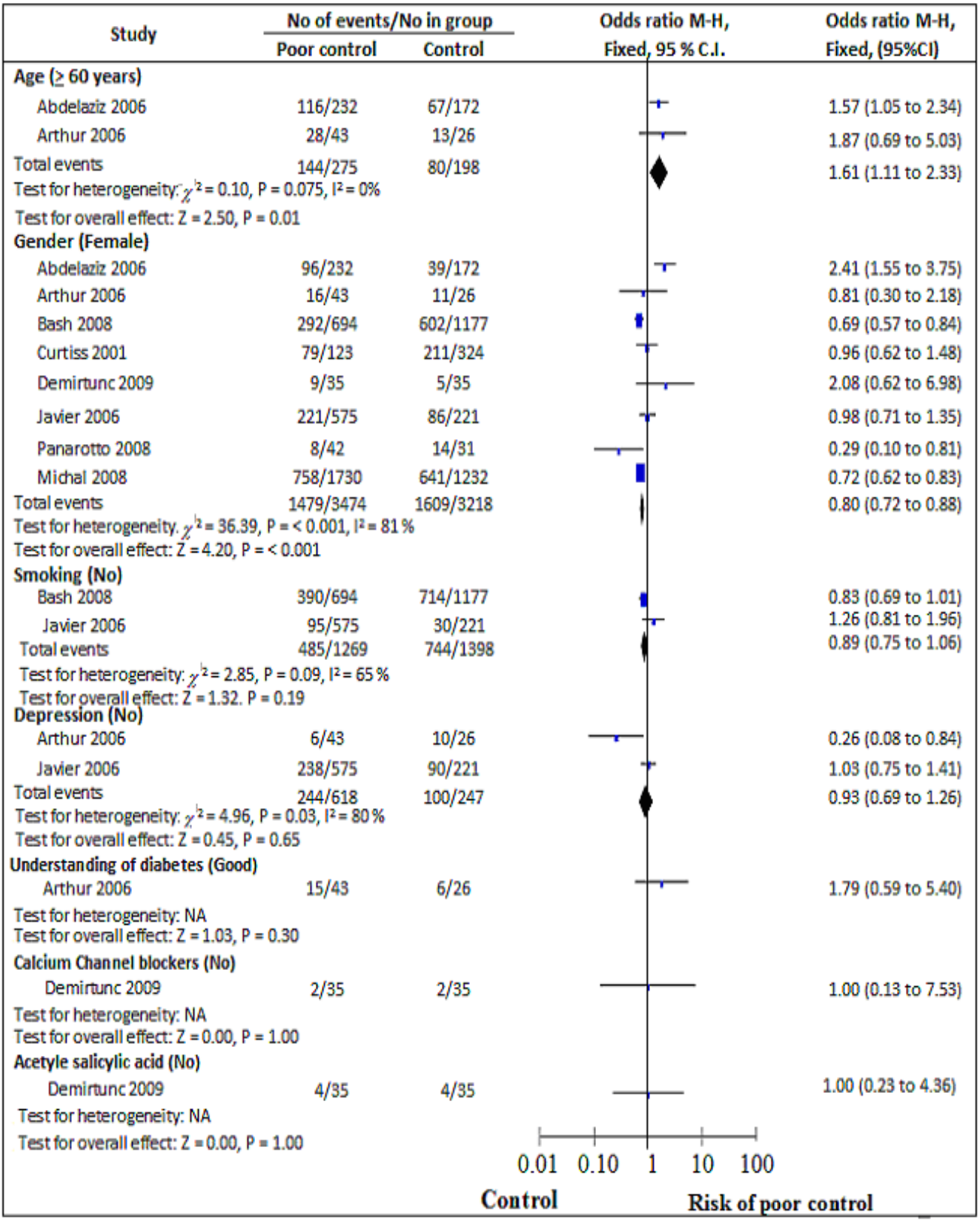


Figure 3. Disease related factors

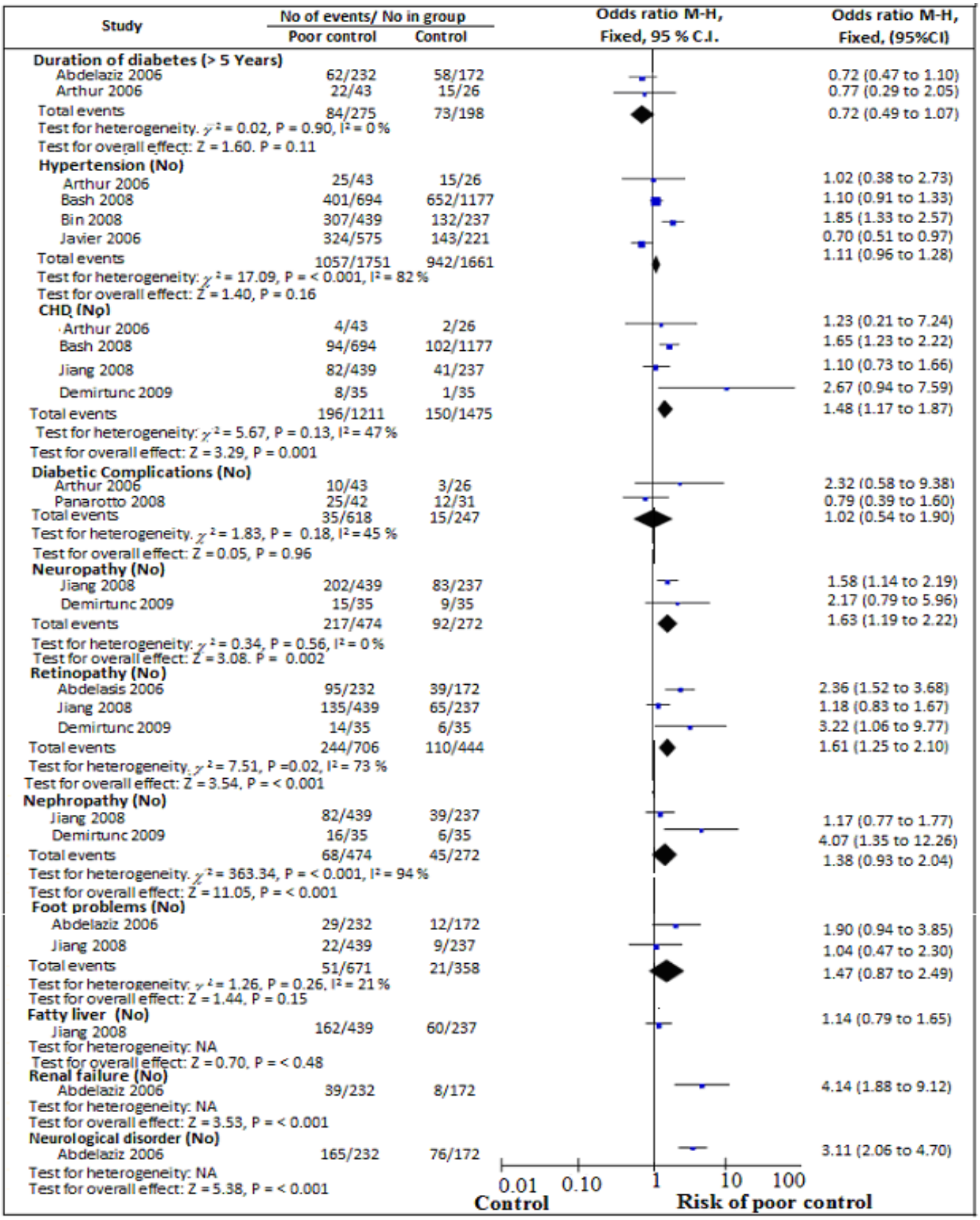
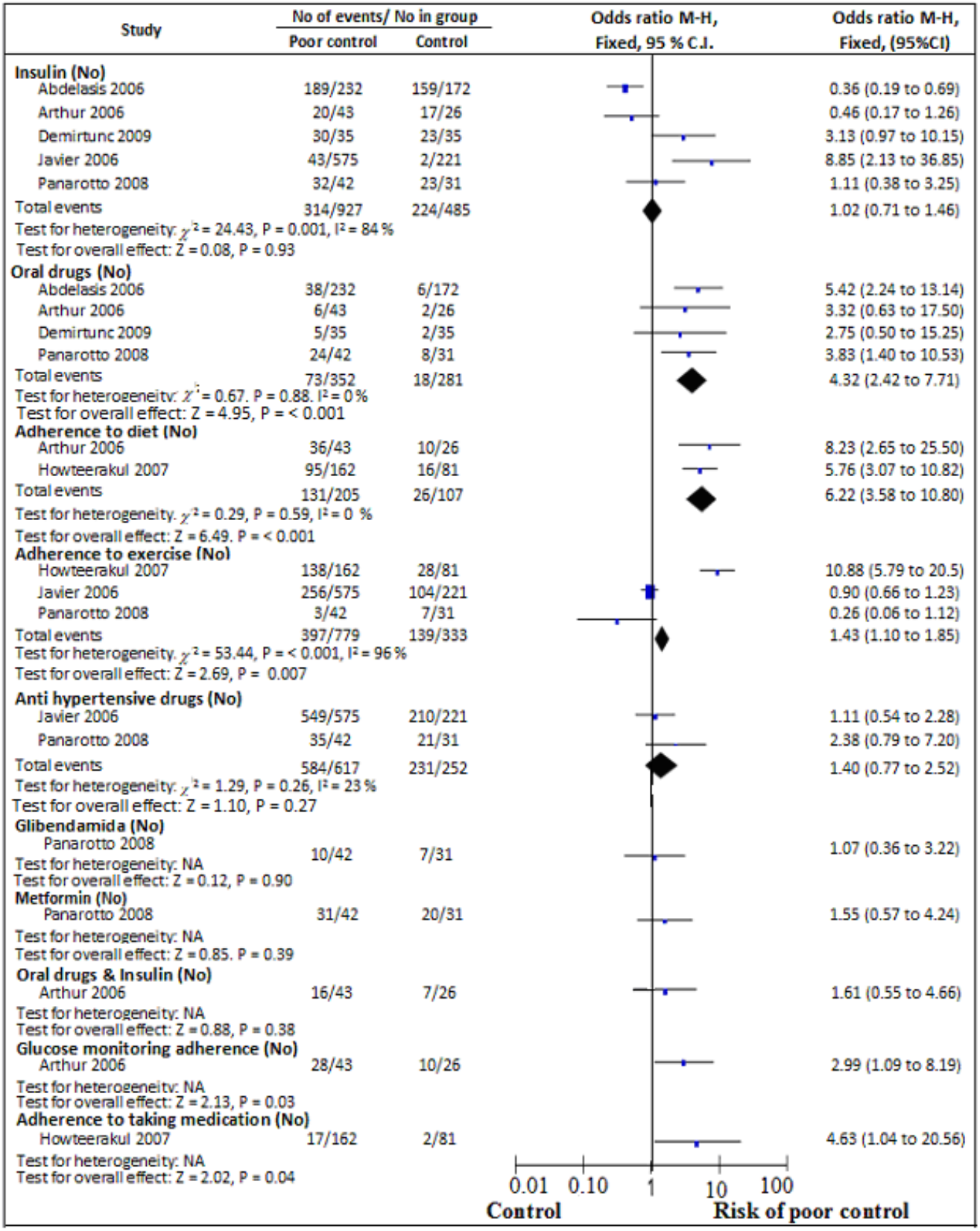


Figure 4. Treatment related factors



Disease related factors

Duration of diabetes, diabetic complications, hypertension, Cornorary Heart Disease (CHD), retinopathy, neuropathy, nephropathy, foot problems, fatty liver, renal failure and neurological disorders were included in disease related factors. Presence of CHD (M.H. O.R.= 1.48, 95 % C.I. = 1.17 to 1.87), neuropathy (M.H O.R = 1.63, 95 % C.I. = 1.19 to 2.22), retinopathy (M.H. O.R. = 1.61, 95 % C.I. = 1.25 to 2.10), renal failure (M.H. O.R. = 4.14, 95 % CI. = 1.88 to 9.12), neurological disorders (M.H. O.R. = 3.11, 95 % C.I. = 2.06 to 4.70) were associated with poor control of diabetes. Duration of diabetes (M.H. O.R. = 0.72, 95 % C.I. = 0.49 to 1.07), medication compliance, fatty liver as well as foot problems were not associated with poor control of diabetes. Meta-analysis results of disease related factors are shown in figure 3.

Treatment related factors

Insulin, oral drugs, adherence to diet and exercise, antihypertensive drugs, glibendamide, metformin, adherence to glucose monitoring and adherence to taking medication were included in treatment related factors. Surprisingly, adherence to diet (M.H. O.R. = 6.22, 95 % CI. = 3.58 to 10.82), adherence to exercise (M.H. O.R. = 1.43, 95 % CI. = 1.10 to 1.85) and intake of oral drugs (M.H. O.R. = 4.32, 95 % CI. = 2.42 to 7.71) were associated with poor control of diabetes. Insulin (M.H. O.R. = 1.02, 95 % CI. = 0.71 to 1.46) and metformin (M.H. O.R. = 1.55, 95 % CI. = 0.57 to 4.24) were not associated with poor control of diabetes. Meta-analysis results of treatment related factors are shown in Figure 4.

Discussion

We have conducted this systematic review to summarize the factors associated with poor control of diabetes. Ten studies qualified for Meta-analysis. Life style modification is one of the major determinants of diabetes control. In our review elderly patients having (> 60 years), males and having normal BMI patients had better control on diabetes. Probably, younger diabetics did not care about the disease control. Usually, the females take the disease only as a second priority as compared to males.

Presence of diseases like coronary heart disease, neuropathy, retinopathy, renal failure and neurological disorders was associated with poor control of diabetes. This shows the importance of diabetes control to prevent complications. Foot problems and fatty liver were not related to poor control of diabetes. Probably there could be other factors that are responsible for poor control of diabetes. With the use of insulin, the control of diabetes improves. Metformin reduces insulin resistance, thereby improving diabetes control. Surprisingly, poorly controlled patients were more adhered to diet, exercise, medication and regular glucose monitoring. One of the reasons could be that once these patients notice that their diabetes is poorly controlled, they are more likely to get adhered to the good behavior.

Conclusion

In spite of our sincere attempt to consolidate all studies, which provide evidence for the factors responsible for poor control of diabetes, we could not find this as primary objectives in many well-conducted studies. However, our experience with literature review showed that this area requires more attention of diabetes researchers.

References

1. Shaw JE, Sucre RA, Zimmet PZ. Global estimates for the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010; 87: 4-14.
2. Roglic G, Unwin N. Mortality attributable to diabetes: Estimates for the year 2010. *Diabetes Res* Clin Pract 2010; 87 :15-19.
3. Zhaolan L, Chaowei F, Weibing W, Biao X. Prevalence of chronic complications of type 2 diabetes mellitus in outpatients- a correstional hospital based survey in urban China. HQLO 2010; 8: 62-71.
4. Joshi SR, Das AK, Vijay VJ, Mohan V. Challenges in diabetes care in India: sheer numbers, lack of awareness and inadequate control. JAPI 2008: 56; 443-450.
5. Ramachandran A. Socio economic burden of diabetes in India. JAPI 2007; 55: 9-12.
6. Sarah W, Gojka R, Anders G, Richard S, Hilary K. Global prevalence of diabetes. Diabetes care 2004; 27: 1047-1053.
7. Home P. The challenge of poorly controlled diabetes mellitus. Diabetes Metab 2003; 29: 101-109.

8. Ramser KL, Spraberg LR, George CM, Hamann GL, Vallejo VA, Dorko CS. Physician-pharmacist collaboration in the management of patients with diabetes resistant to usual care. Diabetes spectrum 2008; 21: 209-214.
9. The Joanna Briggs Institute. Comprehensive systematic review training program manual. Adelaide, Australis: The Joanna Briggs Institute 2004.
10. Julian PT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analysis. Brit Med J 2003; 327: 557-560.
11. RevMan web page. www.cc-ims.net/RevMan.
12. Abdelaziz B, Soltane I, Gaha K, Thabet H, Tlili H, Ghannem H. Predictive factors of glycemic control in type 2 diabetes mellitus patients in primary health care. Rev Epidemiol Sante Publique 2006; 54: 443-452.
13. Arthur H, Sarah K, Paul J, Yinghui X, Michael K, Jeanette D. Factors that influence improvement for patients with poorly controlled type 2 diabetes. Diabetes Res Clin Pract 2006; 74: 227-232.
14. Bash LD, Elizabeth S, Michael S, Josef C, Brad CA. Poor glycemic control in diabetes and the risk of incident chronic kidney disease even in the absence of albuminuria and retinopathy. Arch Intern Med 2008; 22: 2440-2447.
15. Curtiss BC, Robert H, Imad EK, David CZ, Daniel LG, Virgina GD, et.al. The potentially poor response to outpatient diabetes care in urban African – Americans. Diabetes care 2001; 24: 209-215.
16. Demirtunc R, Duman D, Melih B, Mustafa B, Mehmet T, Tayfun G. The relationship between glycemic control and platelet activity in type 2 diabetes mellitus. J Diabetes Complicat 2009; 23: 89-94.
17. Howteerakul N, Suwannapong N, Rittichu C, Rawdaree P. Adherence to regimens and glycemic control of patients with type 2 diabetes attending a tertiary hospital clinic. Asia Pac J Pub Health 2007; 19: 43-49.
18. Javier EG, Florence JD, Ana LS, Cecilia CR, Noe PR, Susan CW. The relative effect of self-management practices on glycaemic control in type 2 diabetic patients in Mexico. Chronic illness 2006; 2: 77-85.
19. Jiang Y, Nie L, Jing C. Association of glycosylated hemoglobin A1c control with the complications in type 2 diabetic patiets. J South Med University 2008; 28: 2180-2182.
20. Michal S, Taylor TR, Sholmo V, Alexander L, Rina E, Asher E, et.al. Characteristics of diabetics with poorly glyceic control who achieve good control. JABFM 2008; 21: 490-496.
21. Panartotto D, Roberto A, Schumacher MV. Factors associated with glycemic control in type 2 diabetes. Rev Assoc Med Bras 2008; 54: 314-321.
22. Ahmed AT, Karter AJ, Warton EM, Doan JU, Weisner CM. The relationship between alcohol consumption and glycemic control among patients with diabetes: The Kaiser permanente Northern California Diabetes registry. J Gen Intern Med 2007;23: 275-282.
23. Alex NG, Ronald PS, Peter Z, Rutten HM. Patient characteristics donot predict poor glycaemic control in type 2 diabetes patients treated in primary care: Eur J Epidemiol 2004; 19: 541- 545.
24. Allison BG, Clara B, Robert AP, Caroline K, Amy K, Stuart SJ, et.al. Insulin resistance is a poor predictor of type 2 diabetes in individuals with no family history of disease. Proc Natl Acad Sci 2003; 100: 2725- 2729.
25. Barak G, Hirsch IB. The effects of improved glycemic control on complications in type 2 diabetes: Arch Intern Med 1998; 158: 134-140.
26. Calvert MJ, Richard JM, Freemantle N. Management of type 2 diabetes with multiple oral hypoglycaemic agents or insulin in primary care: retrospective cohort study. Br J Gen Prace 2007; 57: 455-460.
27. Chan WB, Cockram CS. Glycaemic control in type 2 diabetes: the impact of body weight, beta cell function and patient education. Q J Med 2000; 93: 183-190.
28. Cynthia JW, Susan EA, Joseph C, Jackie CF, Jerry HG. Polypharmacy with oral antidiabetic agents: an indicator of poor glycemic control. Am J Manag Care 2006; 12: 435-440.
29. Ciechanowski PS, Hirsch IB, Wayne JK. Interpersonal predictors of HbA1c in patients with type 1 diabetes. Diabetes care 2002; 25: 731-736.

30. Cohen HW, Crandall JP, Hailpern SM, Billett HH. Aspirin resistance associated with HbA1c and obesity in diabetic patients. J Diabetes Complicat 2008; 22: 224-228.

31. David EL, Jaana L, Timo AL, Johan GE, Leo N, Katja W, et.al. Physical activity in the prevention of type 2 diabetes. Diabetes 2005; 54: 158- 165.

32. Glen HM, Richard MH, Jayendra HS, Christopher SW, William CD. A Probabilistic model for predicting hypoglycemia in type 2 diabetes mellitus. Arch Intern Med 2004; 164: 1445- 1450.

33. Goudswaard AN, Stolk RP, Zuithoff NP, Rutten GE. Patient characteristics do not predict poor glycaemic control in type 2 diabetes patients treated in primary care. Eur J Epidemiol 2005; 19: 541-545.

34. Gregory AN, Teresa AH, Kimberly JP, Jonathan BB. Predictors of glycemic control in insulin-using adults with type 2 diabetes. Diabetes care 2000; 23: 273- 277.

35. Gregorio F, Ambrosit F, Manfrini M, Carle F, Testa R, Merante D, et.al. Poorly controlled elderly type 2 diabetic patients: the effects of increasing sulphonylurea dosages or adding metformin. Diabetic med 1999; 16: 1016-1024.

36. Hayley W, Naomi L, Brent T. Executive congnitive impairment detected by simple bedside testing is associated with poor glycaemic control in type 2 diabetes. S Afr Med J 2007; 97: 1074-1076.

37. Imad ME, Curtiss BC, Ziemer DC, Miller CD, Gallina DL, Phillips LS. Association of younger age with poor glycemic control and obesity in Urban African with type 2 diabetes. Arch Intern Med 2003;163: 69- 75.

38. Ismail IS, Nazaimoon WM, Lectcuman R, Singaraveloo M, Pander R, Faridah et.al. Socio demographic determinants of glycaemic control in young diabetic patients in peninsular Malaysia. Diabetes Res Clin Pr 2000; 47: 57-69.

39. James DL, Cynthia CM, Paula GW, Priti IP, Mark NF, Richard SS. Personality correlates of glycemic control in type 2 diabetes. Diabetes care 2000; 23: 1321-1325.

40. Karin MN, Lybbe M, Gayle R. Factors influencing disease self- management among veterans with diabetes and poor glycemic control. SGIM 2007; 22: 442-447.

41. Katherine LT, Odilia IB, Castaneda C. Type 2 diabetes is prevalent and poorly controlled among Hispanic elders of Caribbean origin. Am J Public Health 2000; 90: 1288-1293.

42. Katsuki A, Sumida Y, Urakawa H, Gabazza EC, Murashima S, Morioka K, et.al. Neither homeostasis model assessment nor quantitative insulin sensitivity check index can predict insulin resistance in elderly patients with poorly controlled type 2 diabetes mellitus. J Clin Endocr Metab 2002; 87: 5332-5335.

43. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. J Exp Clin Med 2007; 7: 24-29.

44. Khan S, Lasker SS, Chowdhury TA. Prevalence and reasons for insulin refusal in Bangladeshi patients with poor controlled type 2 diabetes in east London. Diabetic Med 2008; 25: 1108-1111.

45. Kilpatrick ES, Dominiczak MH, Small M. The effects of ageing on glycation and the interpretation of glycaemic control in type 2 diabetes. Q J Med 1996; 89: 307- 312.

46. Lando LJ, Jacqueline MD, Henk FJ, Bouter LM, Robert JH. Moderate alcohol consumption lowers the risk of type 2 diabetes. Diabetes care 2005; 28: 719-725.

47. Michal S, Tomas RT, Shlomo V, Alexander L, Rina E, Asher E, et.al. Evaluating the characteristics of diabetics with poor glycemic control who achieve good control: A cohort study. Unpublished.

48. Nakahara R, Kazuhiro Y, Hiroaki K, Yoko H, Hiroyuki S, Tomifusa K. Prospective study on influence of psychosocial factors on glycemic control in Japanese patients with type 2 diabetes. Psyhosomatics 2006; 47: 240- 246.

49. Odegard PS, Gray SL. Barriers to medication adherence in poorly controlled diabetes mellitus. The diabetes educator 2008; 34: 692-697.

50. Patric JL, Monique MW, Gregory SS, Bill DN, Ray EC. Factors influencing glycemic control in type 2 diabetes during acute and maintenanc phase treatment of major depressive disorder with Bupropion: Diabetes care 2007; 30: 459- 466.

51. Patric JL, Ryan JA, Kenneth EF, Mary D G, Robert M C, Ray E C. Depression and poor glycemic control. Diabetes care 2000; 23: 934-342.

52. Russell R, Robb M, Betsy B, Cheryl H, Michael P. Pharmacist led, primary care- based disease management improves Hemoglobin A1c in high- risk patieits with diabetes. Am J Med Qual 2003; 18: 51-58.

53. Singh R, Press M. Can we predict future improvement in glycaemic control. Diabetic Med 2008; 25: 170-173.

54. Stephen RB, Regina F, Athena PT, Ming J. Predictors of glycemic control among patients with type 2 diabetes: A longitudinal study. BMC Public Health 2005; 5: 36-45.

55. Tahseen AC, Valerie E. Poor glycaemic control caused by insulin induced lipohypertrophy. Brit Med J 2003; 327: 383-384.