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Meeting Report

Risk factors and complications of diabetes

Highlights from the Annual Professional Conference of Diabetes UK, held March 5-7, 2008, in Glasgow, U.K.

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CONTENTS

Abstract

Diabetes UK held its annual professional conference on March 5-7, 2008, in Glasgow, U.K. The meeting was devoted to developments in different areas of diabetes, including basic and clinical science, treatment options, risk factors, complications and healthcare delivery and improvement.

Introduction

Diabetes is a complex metabolic condition that requires meticulous management and a global approach. Poor management and control of diabetes often lead to poor disease outcomes. The management of diabetes and its complications presents an increasing challenge to healthcare systems throughout the world. New findings regarding complications of diabetes, their prevalence and incidence, and risk factors involved were discussed at the Annual Professional Conference of Diabetes UK, held March 5-7, 2008, in Glasgow, U.K.

Diabetic nephropathy

Diabetes and hypertension are major risk factors for the development of end-stage renal disease. Increased albumin excretion is seen in the early stage of diabetic nephropathy before the glomerular filtration rate decreases. Microalbuminuria, macroalbuminuria and end-stage renal disease are all associated with an increased risk of death. People with chronic kidney disease have a greater risk of developing cardiovascular disease and diabetes, as seen in a multiethnic population (1).

Patients with type 2 diabetes are at risk of developing chronic kidney disease. The isotopic glomerular filtration (iGFR) rate was measured in type 2 diabetic patients at diagnosis and then at regular intervals over the next 10 years. It was found that there was a marked decrease in iGFR in the first year of diagnosis of type 2 diabetes, followed by a subsequent more modest rate of decline in GFR (2).

Cardiovascular disease

Cardiovascular disease is the main cause of mortality in patients with diabetes, and risk reduction is an important goal in the treatment of diabetes. In individuals, little is known about the importance of progressive change or variability over time in risk factors for atherosclerotic vascular disease. Data have shown a significant increase for major cardiovascular events and procedures in subjects with type 2 diabetes, which has important financial and health-planning considerations for the future (3).

Endothelial dysfunction, carotid intima-media thickness (CIMT) and lipoprotein abnormalities are factors contributing to cardiovascular disease. One study found that abnormalities in flow-mediated dilatation and CIMT are present in young type 1 diabetic patients and correlate well with lipoprotein abnormalities (4). The PREDICT study measured the coronary artery calcification score (CACS) and found it to be a powerful predictor of cardiovascular events in asymptomatic patients with type 2 diabetes (5).

Both metabolic syndrome and type 2 diabetes are associated with a high cardiovascular risk due to clustering of atherothrombotic risk factors such as insulin resistance, dyslipidemia, hypertension, hypercoagulability and dysglycemia. Insulin resistance in type 2 diabetic patients may be responsible for hypertension and dyslipidemia. A

study by Petrie *et al*. concluded that prehypertension is associated with obesity but not specifically with insulin resistance or metabolic syndrome (6). Although the majority of type 2 diabetic patients are obese, the body mass index was found to be a poor discriminator of cardiovascular risk in these patients (7).

Ischemic heart disease (IHD) is the most frequent macroangiopathic complication and the main cause of death in subjects with type 2 diabetes. Myocardial infarction often occurs in type 2 diabetic patients with no previous cardiac symptoms. Diabetes is an important determinant of death after acute myocardial infarction (AMI) and adversely affects the outcome after AMI (8). Another study found hypertension to be a risk factor for IHD in a Scottish type 1 diabetic population and high-density lipoprotein (HDL) was found to have a protective effect against cardiovascular disease (9).

Endothelial dysfunction leads to atherosclerosis, which is the leading cause of macrovascular complications and death in patients with type 2 diabetes. Investigations within the endothelium have been limited by access until the recent development of a new technique to sample cells from a forearm vein in humans. Howie *et al.* supported the idea of obtaining the sample from a superficial vein, allowing evaluation of molecular events in small quantities of human vascular cells (10).

Type 2 diabetes is associated with increased vascular superoxide levels and impaired endothelial function. Researchers from Glasgow examined the effect of diabetes on vascular superoxide production in patients undergoing coronary artery bypass graft. They concluded that reduced superoxide production in patients with type 2 diabetes may be attributable to increased use of modifiers of the angiotensin system and oral hypoglycemic agents. Thus, other factors such as impaired smooth muscle function and reduced endothelial nitric oxide generation may be responsible for impaired endothelium-dependent vasorelaxation in diabetes (11).

Individuals with features of metabolic syndrome and an increased risk of cardiovascular disease are found to have reduced functional vasodilatory reserve and this impaired response may contribute to decreased insulin sensitivity and glucose uptake by muscle (12). Oxidative stress markers such as whole-blood reduced glutathione and the ratio of reduced and oxidized glutathione may be integrally related in the etiology of the vasculopathy exhibited by type 2 diabetic patients (13). Another interesting survey suggested that arterial function deteriorates more rapidly in mothers with gestational diabetes and continues to do so postpartum, despite resolution of glucose intolerance (14).

Angiogenesis occurs within atherosclerotic plaques and a study investigated the effects of thrombin on key aspects of angiogenesis such as cell proliferation, vascular tubule formation and expression of pro- and antiangiogenic regulators. The investigators found that thrombin stimulates vascular smooth muscle cell proliferation, but attenuates endothelial cell-mediated growth of vascular tubules and branching of new vascular structures (15).

Osteoprotegerin, an antiresorptive agent in bone, is present in the systemic vasculature. It is normally high after menopause as a compensatory mechanism for excessive bone turnover. The level of osteoprotegerin is also high in type 2 diabetic patients. The earlier rise and loss of the normal postmenopausal rise may represent an underlying premature vascular inflammatory process in diabetic patients (16).

Adiponectin is an adipocytokine with favorable metabolic and vascular effects. High adiponectin levels are consistently associated with a lower diabetes risk. However, evidence from studies linking total adiponectin and vascular disease indicate no clear association. A study from Nottingham assessed the effects of adiponectin on endothelial cell proliferation and angiogenesis *in vitro* and found that low concentrations of adiponectin stimulate angiogenesis and exert antiapoptotic effects on endothelial cells (17). Another study, however, did not find any association between high-molecular-weight adiponectin levels and incident coronary heart disease events (18).

Diabetic neuropathy

Neuropathy in diabetic patients is a major source of morbidity. The pathogenesis of diabetic neuropathy remains poorly understood. Diabetic peripheral neuropathy is a common and debilitating consequence of diabetes. There are established risk factors for the development of peripheral neuropathy in patients with diabetes, such as poor glycemic control and hypertension. Increasing subject height was found to be associated with an increased long-term risk of developing neuropathy in type 1 diabetic patients who participated in the DCCT follow-up study (19). In type 1 diabetic patients, the additional diagnosis of celiac disease appears to lead to poorer nerve conduction even when controlling for glycemic control (20).

Depression may be a major confounder of outcomes in clinical trials in diabetic peripheral neuropathy. Subjects with even moderate levels of depression are more likely to have higher baseline pain scores and to respond favorably to any intervention, whether placebo or active (21).

Although there is an increased propensity for the development of carpal tunnel syndrome in people with diabetes, the basis for this has not been established. Increased upregulation of hypoxia-inducible factor 1 α (HIF-1α), vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor 2 (VEGFR2), suggestive of increased hypoxia and vascular permeability, was found in diabetic patients with established carpal tunnel syndrome (22).

In an animal study, glycation adducts were found in the extracellular matrix of the sciatic nerve of streptozotocin-induced diabetic rats, which may contribute to decreased regeneration of sensory neurons, leading to peripheral neuropathy (23).

The accurate quantification of diabetic neuropathy is important to define at-risk patients and anticipate deterio-

ration. Corneal confocal microscopy is a rapid, noninvasive technique that has been shown to be a reliable surrogate measure of somatic neuropathy and found to be useful in diagnosing and following the progression of diabetic neuropathy in relation to risk factors (24). A study from London revealed that Contact Heat Evoked Potential Stimulator, which is a practical, rapid and noninvasive clinical tool, can be used to evoke recordable potentials for the diagnosis of small-fiber neuropathy (25). Another study suggested that mRNA for neuron-specific enolase may be a useful marker for diabetic neuropathy (26).

Autonomic neuropathy is another important complication of diabetes that is associated with increased mortality. However, it is often not diagnosed until advanced symptoms occur. Spectral analysis of heart rate variability is a novel technique that detects autonomic dysfunction in diabetes in the very early stages. It can also be used as a measure of peripheral neuropathy, as well as a marker of long-term risk (27). Spectral analysis of heart rate variability and baroreceptor sensitivity in combination may detect early autonomic dysfunction in young adults with type 1 diabetes (28).

Diabetic retinopathy

Digital retinal screening was performed in both type 1 and type 2 diabetic patients to measure the prevalence of diabetic retinopathy. The prevalence rate for diabetic retinopathy in type 2 diabetic patients on oral hypoglycemic drugs appeared to be lower than in other population studies. Visual acuity was well preserved and type 2 diabetic patients receiving insulin were at high risk of diabetic retinopathy, particularly maculopathy (29). A retrospective analysis found that the prevalence of sight-threatening maculopathy is highest in eyes with sight-threatening diabetic retinopathy and negligible in eyes with screen-negative retinopathy (30).

A study from London indicated that sleep-disordered breathing, which is quite common in type 2 diabetic patients, plays an etiological role in diabetic retinopathy (31). Another study mentioned that sleep-disordered breathing may play a role in metabolic syndrome via the inflammatory pathway (32).

Hypoglycemia

Hypoglycemia is a common adverse event of diabetes treatment and remains a major barrier to achieving optimal glycemic control in both type 1 and type 2 diabetic patients, particularly those who are on insulin. Hypoglycemic episodes may compromise the patients' quality of life. Bedtime blood glucose is a significant risk factor for nocturnal hypoglycemia in type 1 diabetic subjects and these subjects did not show any rebound hyperglycemia following nocturnal hypoglycemia (33). Gill *et al.* found that all the nocturnal hypoglycemic episodes in patients with type 1 diabetes were associated with tachycardia and a subgroup appeared prone to develop bradycardia, which may be responsible for sudden death (34). Researchers documented a wide range of Q-T lengthening following inhaled salbutamol in type 1 diabetic patients. These results can be compared with the responses during experimental hypoglycemia to establish it as a screening test for those at risk of abnormal cardiac repolarization leading to fatal cardiac arrhythmias during severe nocturnal hypoglycemia (35).

Type 1 diabetic patients are likely to be unaware of hypoglycemia because of impairment of the protective neurohumoral counterregulatory responses to impending hypoglycemia due to repeated hypoglycemic episodes. Impaired awareness of hypoglycemia (IAH) is thought to affect approximately 25% of subjects with type 1 diabetes. Despite improvements in insulin therapies, intensification of insulin regimens and innovative patient education, a survey of a large hospital-based clinical population confirmed that 19.5% of type 1 diabetic patients continue to have IAH (36). Two different studies from the same group of investigators reported that patients with IAH had a 3-fold higher incidence of severe hypoglycemia (37), a 2-fold increase in mild biochemical hypoglycemia and a 7-fold increase in the incidence of episodes of asymptomatic hypoglycemia compared to type 1 diabetic patients with normal awareness (38). In contrast, IAH in insulin-treated type 2 diabetic patients is less common as a clinical problem. However, those with IAH have an increased risk of both mild and severe hypoglycemia (39).

Metabolic syndrome

The metabolic syndrome increases cardiovascular risk in type 2 diabetes. Abdominal adiposity is considered a major risk factor for type 2 diabetes, metabolic syndrome and cardiovascular diseases. This is supported by Yang *et al.,* who found that visceral adiposity remains a strong and significant determinant of insulin resistance in WHO grade III obesity. Neck circumference rather than subcutaneous fat is a more reproducible and precise measurement in this severely obese cohort (40). An association between increased central obesity and lower serum adiponectin and an intimate relationship between triglycerides and insulin resistance were found in schizophrenic patients treated with clozapine. Changes in waist-hip ratio over time may result in abnormal glucose handling and routine measurement of this parameter is necessary in this group of patients (41). Another study suggested that plasma triglycerides and the albumin:creatinine ratio are associated with type 2 diabetes in morbid obese subjects (42).

Musculoskeletal disease

Early detection of microvascular and macrovascular complications in subjects with diabetes could prevent fatal outcomes. Locomotor disease is found in 57% of patients with type 1 diabetes. Capsulitis invariably coexisted with other upper limb abnormalities and predicted the presence of retinopathy and/or neuropathy. The mean glycosylated hemoglobin (HbA1c) was also higher in

patients with shoulder problems and these results are very similar to those found in type 2 diabetic patients (43). Another study found that the presence of diabetic peripheral neuropathy, retinopathy and nephropathy was significantly higher in patients with limited joint mobility (44). Therefore, all diabetic patients should be clinically examined for upper limb locomotor disease and limited joint mobility, and if present, they should be evaluated further for other diabetic complications.

Other risk factors

Chronic liver disease is a major cause of morbidity and mortality. Up to 75% of subjects with type 2 diabetes have nonalcoholic fatty liver disease at diagnosis. A secondary-care prevalence study revealed that 20% of patients with diabetes had elevated alanine aminotransferase (ALT), γ-glutamyltranspeptidase (GGT), or both (45). An audit found that a significant proportion of both men and women with poor glycemic control have abnormal lipid profiles associated with a very high risk of cardiovascular disease (46).

Coronary heart disease (CHD), diabetes and chronic kidney disease together are considered a 'deadly trio' and an audit by the Deadly Trio Project found that 90% of the patients were not receiving the optimal standard care (47). This project identified men at high risk of CHD mortality, including all with known diabetes, and ensured that all will be offered appropriate treatment (48). Another similar study from Spain found that type 2 diabetic patients who are not well controlled with two or more oral antidiabetic drugs have altered metabolic profiles, with HbA1c levels in the range requiring immediate intervention. Cardiovascular risks in these patients were high, with the coexistence of other risk factors (49).

Ethnic variation

The incidence of diabetes and its complications varies in different ethnic populations. A cross-sectional survey revealed higher plasma glucose, serum leptin, von Willebrand factor, tissue plasminogen activator and fat mass-bioimpedence in South Asian children compared with Europeans, which make an important contribution to the differences in insulin resistance observed in these populations (50). Another similar study found higher mean truncal skinfold thickness, HbA1c, fasting insulin and triglycerides, and lower HDL cholesterol in South Asian children compared with age-adjusted white Europeans (51). Purmah *et al.* found that the prevalence of microvascular complications such as retinopathy, nephropathy and neuropathy and mean HbA1c are significantly higher and the use of metformin, sulfonylureas and insulin is significantly lower in India compared to Mauritius and the U.K. (52). Poor glycemic control in South Asian subjects with type 2 diabetes and chronic disease comorbidity may be responsible for the increased risk of mortality and morbidity (53). Although a higher proportion of South Asians were found to have poor glycemic control, the prevalence of obesity, smoking and hypertension was lower in this group than in non-South Asians (54). Therefore, there may be important opportunities for the early prevention of type 2 diabetes and other microvascular and macrovascular complications in this high-risk ethnic group.

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References

1. Crasto, W., Srinivasan, B.T., Jarvis, J. et al. *The influence of chronic kidney disease (CKD) on cardiovascular disease (CVD) risk factors in a multi-ethnic UK population.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P264.

2. Chudleigh, R.A., Dunseath, G., Peter, R. et al. *A 10-year, longitudinal study of glomerular filtration rate in subjects with type 2 diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A17.

3. Millett, C., Bottle, A., Underwood, J., Khunti, K., Majeed, A. *Trends in cardiovascular admissions and procedures for people with and without diabetes in England: 1996-2005*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A43.

4. Sibal, L., Jones, A., Neely, D. et al. *Endothelial dysfunction, CIMT and lipoproteins in young people with type 1 diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A40.

5. Elkeles, R.S., Godsland, I.F., Feher, M.D. et al. *A prospective cohort study to evaluate the role of coronary calcium in predicting cardiovascular events in asymptomatic patients with type 2 diabetes: Results of the PREDICT Study*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A42.

6. Petrie, J.R., Melander, O., Perry, C.G., Natali, A. *Prehypertension is associated with central obesity but not specifically with insulin resistance/metabolic syndrome*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A41.

7. Song, S.H., Hardisty, C.A. *BMI is a poor discriminator of cardiovascular risk in type 2 diabetes.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P78.

8. Ramachandra, R., Dudley, F., Batin, P.D., Wilson, J.I., Gale, C.P. *Outcome after myocardial infarction in patients with diabetes: A real world experience*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P77.

9. Shah, I.M., Collier, A. *Cardiovascular disease and risk factors in a UK type 1 diabetic population.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P86.

10. Howie, J., Sutherland, C.D., Lang, C.C. *Molecular variations between aortic and venous endothelial cells.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P29.

11. Dymott, J.A., Owala, F.O., Hamilton, C.A. et al. *Reduced vascular superoxide production in patients with coronary artery disease (CAD) and type 2 diabet*es. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P25.

12. L'Esperance, V.S., Turzyniecka, M., Krentz, A.J., Byrne, C.D., Clough, G.F. *Decreased microvascular functional vasodilatory reserve and features of the metabolic syndrome*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P26.

13. Cummings, M.H., Kar, P., Laight, D., Shaw, K.M., Allard, S. *Associations between novel markers of cardiovascular risk in a type 2 diabetic population*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P24.

14. Quin, A.J., Cruickshank, J.K., Stuart-Buttle, C., Banerjee, M. *The effects of pregnancy on arterial stiffness markers in mothers with glucose intolerance*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P28.

15. Wang, B., Atherton, P., Manning, G., Donnelly, R. *In-vitro effects of thrombin on tubule formation and regulators of angiogenesis.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P16.

16. O'Sullivan, E.P., Ashley, D.T., Devlin, N. et al. *Osteoprotegerin rises earlier in type 2 diabetes and is correlated with underlying vascular inflammation.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P13.

17. Wang, B., Atherton, P., Manning, G., Donnelly, R. *Adiponectin is pro-angiogenic and has anti-apoptotic effects on endothelial cell*s. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P5.

18. Watt, P., Cherry, L., Lawlor, D. et al. *High molecular weight adiponectin and incident coronary heart disease in older women: Findings from a prospective case control study nested within the British Women's Heart Health study.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A31.

19. Kilpatrick, E.S., Rigby, A.S., Atkin, S.L. *The effect of subject height on the long term risk of neuropathy in type 1 diabetes: An analysis of the EDIC cohort*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A46.

20. Leeds, J.S., Sanders, D.S., Hadjivassiliou, M., Tesfaye, S. *Coeliac disease confers additional risk to peripheral nerve function in type 1 diabetes mellitus*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P59.

21. Selvarajah, D., Gandhi, R., Bowler, H., Emery, C.J., Tesfaye, S. *Future clinical trial in painful diabetic neuropathy should account for depression as a major confounder of outcomes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P57.

22. Ali, R., Mojaddidi, M., Jeziorska, M. et al. *Molecular basis for the increased risk of carpal tunnel syndrome in people with diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A44.

23. Gardiner, N.J., Moffatt, S., Dobler, D. et al. *Formation of advanced glycation endproducts in the extracellular matrix of rat sciatic nerve: Contribution to failure of sensory nerve regeneration*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P18.

24. Das, T.J., Tavakoli, M., Iqbal, A. et al. *Corneal confocal microscopy to assess progression of diabetic neuropathy: A longitudinal study in people with diabetes over 5 years.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A45.

25. Narayanaswamy, H., Roberts, K., Anand, P. *Use of the novel Contact Heat Potential Stimulator (CHEPS) for the diagnosis of small fibre neuropathy: 75 patients*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P56.

26. Sandhu, H.S., Butt, A.N., Powrie, J., Swaminathan, R. *Blood marker for diabetic neuropathy*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P54.

27. Gandhi, R.A., Marques, J., Selvarajah, D., Emery, C.J., Tesfaye, S. *Spectral analysis of heart rate variability correlates strongly with measures of peripheral nerve function and traditional risk markers in diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A77.

28. Marques, J.L.B., Robinson, E.J., Emery, C.J. et al. *Detection of subclinical autonomic dysfunction in young adults with type 1 diabetes based on spectral analysis of heart rate variability and baroreflex sensitivity*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A66.

29. Osman, A., Brooks, A.P., Li Voon Chong, J.S.W., Hall, N., Watts, J.A. *Prevalence and risk of diabetic retinopathy (DR) varies with type of diabetes as shown by a digital retinal screening service*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P353.

30. Mendis, B., Lindsay, H., Meredith, S., Duffy, J., Idris, I. *Association between the prevalence of maculopathy and grades of diabetic retinopathy (DR). North Nottinghamshire Diabetic Retinopathy Screening Programme*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P352.

31. Merritt, S., Wong, A., Carroll, P. et al. *Sleep disordered breathing, a causative factor in the development of severe diabetic retinopathy?* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A94.

32. Brady, E.M., Davies, M.J., Hall, A.P. et al. *Sleep disordered breathing is independently associated with the metabolic syndrome in a multi-ethnic population: An inflammatory link?* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A65.

33. Woodward, A., Casson, I., Weston, P., Gill, G.V. *Bedtime blood glucose predicts nocturnal hypoglycaemia in type 1 diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P38.

34. Gill, G.V., Groves, D., Fisher, A.C. et al. *Nocturnal hypoglycaemia in type 1 diabetes: The relationship with bradycardia and implications for the 'dead in bed' syndrome.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P39.

35. Robinson, E.J., Marques, J.L.B., Downes, J.J. et al. *Developing a simple test to identify those at most risk of abnormal cardiac repolarisation during hypoglycaemia.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P40.

36. Schopman, J., Geddes, J., Zammitt, N.N., Frier, B.M. *Prevalence of impaired awareness of hypoglycaemia in adults with type 1 diabetes.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P192.

37. Choudhary, P., Geddes, J., Heller, S.R., Frier, B.M. *Determining the increased risk of severe hypoglycaemia in patients with impaired awareness of hypoglycaemia*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P196.

38. Geddes, J., Wright, R.J., Zammitt, N.N., Frier, B.M. *Frequency of biochemical and asymptomatic hypoglycaemia in people with type 1 diabetes – with and without impaired awareness of hypoglycaemia.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P193.

39. Schopman, J., Geddes, J., Frier, B.M. *Awareness of hypoglycaemia in people with insulin-treated type 2 diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P195.

40. Yang, L.Y., Samarasinghe, Y.P., Al-Zaman, Y., Amiel, S.A., Aylwin, S.J.B. *Visceral adiposity remains a primary determinant of insulin resistance even in morbid obesity*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P61.

41. Heald, A.H., Anderson, S.G., Hanssens, L., de Hert, M. *Waist-hip ratio most closely predicts raised blood glucose in individuals with clozapine treated schizophrenia.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P62.

42. Khanolkar, M.P., Gripper, H., Lawson, T., Price, D.E., Stephens, J.W. *Clinical determinants of diabetes susceptibility in morbidly obese subjects.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P60.

43. Ramchurn, N., Mashamba, C., Kelly, C. et al. *The prevalence and relevance of upper limb musculoskeletal disease in type 1 diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P259.

44. Kumaravel, V., Huber, J., Kumar, H. et al. *Association of limited joint mobility and diabetic microvascular complication.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P260.

45. Kejariwal, D., Scovell, L., Freeman, K., Phillips, M., Dhatariya, K. *Abnormal liver function tests and diabetes mellitus – A secondary care prevalence study*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A97.

46. Oluwatowoju, I.O., Abu, E.O., Byrne, C.D. *An audit of plasma lipid concentration in adults with diabetes and poor glycaemic control*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P70.

47. Ahmed, S., Burden, A.C.F., Rouse, A., Chambers, J., Taylor, B. *Deadly trio: Coronary heart disease, diabetes mellitus and chronic kidney disease – A mega audit*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P92.

48. Burden, A.C.F., Rouse, A., Chambers, J. et al. *Why have coronary heart disease deaths not fallen in deprived inner cities: Can this be improved with the Deadly Trio programme?* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P88.

49. Calderon, A., Sarasa, P., Barrios, V. *Metabolic profile and cardiovascular risk in patients with type 2 diabetes not controlled with oral antidiabetic agents: Post-Adelante study.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P91.

50. Whincup, P.H., Kaye, S., Owen, C.G. et al. *Body composition, markers of type 2 diabetes and cardiovascular risk among South Asians: New evidence from a study of adolescents.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A62.

51. Whincup, P.H., Owen, C.G., Musonda, P. et al. *Ethnic differences in type 2 diabetes and insulin resistance originate in early life: Evidence from a study in British children.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst A60.

52. Purmah, Y.J., Dowlut, M.S., Sewpaul, N., Potluri, R. *Microvascular diabetic complications are more prevalent in India compared to Mauritius and the UK due to poorer diabetic control.* Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P157.

53. Khunti, K., Mehta, R., Ali, S. et al. *Impact of chronic disease comorbidity on glycaemic control in a multi-ethnic population with type 1 and type 2 diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P158.

54. Wild, S.H., McConnachie, A.M., Lindsay, R.S. *Prevalence of cardiovascular disease risk factors among South Asians and non-South Asians with diabetes*. Annu Prof Conf Diabetes UK (March 5-7, Glasgow) 2008, Abst P93.