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ORIGINAL ARTICLE

Impact of preexisting diabetes mellitus on transplantation outcomes in hematopoietic stem cell transplantation

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Abstract

New onset diabetes mellitus is frequently observed following hematopoietic stem cell transplantation (HSCT) and is associated with adverse transplantation outcomes. However, the outcomes of patients with preexisting diabetes mellitus undergoing HSCT are largely unknown. We aimed to explore the impact of preexisting diabetes on transplantation outcomes in HSCT. In a retrospective study, medical charts of 34 HSCT recipients with diabetes mellitus undergoing allogeneic or autologous transplantation were reviewed and compared with 71 HSCT recipients without diabetes. Primary outcome was overall survival. Secondary outcomes included hematopoietic recovery, length of hospital stay, febrile neutropenia, acute and chronic graft-versus-host disease (GVHD), primary disease recurrence, and non-relapse mortality (NRM). On univariate analysis, there was no difference in transplantation outcomes in recipients with diabetes compared with recipients without diabetes. However, after adjusting for potential covariates, multivariate analysis demonstrated that having diabetes before HSCT significantly predicted outcome and decreased overall survival (hazard ratio 0.51, 95% confidence interval: 0.27–0.97, *p* value: 0.04). This study suggests that patients with diabetes mellitus undergoing allogeneic or autologous HSCT may have inferior survival rates and warrant further attention.

Keywords

Febrile neutropenia, neutrophil engraftment, overall survival, platelet engraftment, post-transplantation hyperglycemia, Pre-transplant fasting plasma glucose

History

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Introduction

Hyperglycemia is a frequent observation following hematopoietic stem cell transplantation (HSCT) (1). Stress-induced hyperglycemia, immunosuppression, receiving steroids for the treatment of graft-versus host disease (GVHD), and receiving total parenteral nutrition (TPN) are among the factors which contribute to post-transplantation hyperglycemia in this population (2–7). In addition to hyperglycemia, new-onset diabetes mellitus is also a frequent observation following HSCT (8–11).

In the setting of HSCT, several studies have illustrated that post-transplantion hyperglycemia and diabetes can adversely affect transplantation outcomes including overall survival (OS), non-relapse mortality (NRM), length of hospital stay, organ function, and GVHD (1,3–8,12). In this regard, hyperglycemia due to glucocorticoid therapy for acute GVHD has been shown to adversely affect OS and NRM (7). Likewise, TPN-induced hyperglycemia denotes an increased risk of infections (3,4) and increased time to neutrophil and platelet recovery (4).

In contrast to bulk of the literature evaluating the effect of post-transplant hyperglycemia and diabetes, the influence of pre-transplant diagnosis of diabetes on HSCT outcomes is largely unknown. Of note, pre-transplant diabetes mellitus is demonstrated to be an outcome predictor following solid organ transplantations (13–19). Lower survival rates have been described in the setting of heart (13) as well as kidney (18) recipients with diabetes. Additionally, it has been suggested that preexisting diabetes influences morbidity and mortality after liver transplantation (14–15,17).

Therefore, the independent impact of pre-transplant diabetes in the setting of HSCT merits investigation. In the present study, we aimed to delineate early and long-term outcomes among diabetic recipients undergoing autologous or allogeneic HSCT.

Methods

Data source

This retrospective cohort study was performed in the Hematology-Oncology, Bone Marrow Transplantation

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Research Center at Shariati Hospital, Tehran University of Medical Sciences (TUMS). We reviewed all adult patients' records undergoing HSCT since center establishment on March 1991 up to July 2011 to identify those with pre-transplantation diagnosis of diabetes. Data of hematopoietic recipients with preceding diabetes as well as a control group of age and sex matched HSCT recipients without prior diabetes were collected for this study. This study was approved by TUMS ethic committee.

Patient selection and definitions

Studied population consisted of HSCT recipients who had undergone autologous or allogeneic transplantation and had a prior to transplantation diagnosis of diabetes mellitus. Diabetes was defined as fasting plasma glucose (FPG) $\geq$6.99 mmol/L, according to the criteria of American Diabetes Association (20).

In addition, allogeneic HSCT recipients were included if (i) had received peripheral blood as stem cell source, (ii) had received grafts from HLA-matched sibling donors, and (iii) had received a myeloablative conditioning regimen. Patients were excluded if they had any of the following: (i) had received irradiation in the preparative regimen and (ii) undergoing re-transplantation.

A control group of HSCT recipients with the above criteria but without pre-transplant diagnosis of diabetes were also assigned. In this study, we compared outcomes in two different groups of diabetic and non-diabetic patients.

Recipients received conditioning regimen according to the standard protocols based on the primary disease requiring transplantation and the setting: allogeneic versus autologous HSCT. Allogeneic HSCT recipients received prophylactic therapy for acute GVHD with cyclosporine and methotrexate. Cyclosporine dose was adjusted based on the trough serum levels of 83–333 nmol/L. Beta thalassemia major recipients also received equine antithymocyte globulin.

Supportive care was provided as indicated. Antibiotics were commenced empirically in cases of febrile neutropenia. Other supportive measures such as blood products, granulocyte colony stimulating factor, and TPN were prescribed accordingly.

FPG was measured at least daily in recipients with diabetes and three times a week in patients without diabetes.

Study end points

Primary outcome included OS. Secondary outcomes included neutrophil and platelet engraftment, length of hospital stay, febrile neutropenia, acute and chronic GVHD, primary disease recurrence or relapse, and NRM. Acute and chronic GVHD were assessed in patients undergoing allogeneic transplantation. Hematopoietic recovery, febrile neutropenia, and acute GVHD were assessed and compared between the two groups during the length of hospital stay, defined as the time period of transplantation to discharge. Likewise, incidence of chronic GVHD, relapse/recurrence, survival, and NRM were reported in the time period of last patient follow-up in clinic till July 2011 and, therefore, compared between the two groups in this time frame.

Neutrophil engraftment was defined as the first of three consecutive days after transplantation that the absolute neutrophil count exceeded 0.5×10^9/L. Platelet engraftment was defined as the first day of three consecutive days with platelet count above 20×10^9/L without transfusion. NRM was defined as mortality due to transplant complications and OS as the time elapsed from transplantation to death from any cause.

Statistical analysis

We have reported continuous variables as mean $\pm$ SD. The distribution of continuous variables was assessed by the Kolomogrov–Smirnov test. To compare continuous variables between the group of patients with diabetes and the control group, independent sample *t*-test or the Mann–Whitney *U* test was applied to analyze the significance of difference. Categorical variables between the diabetic and control groups were compared using the Chi-square test or the Fisher exact test as appropriate. Probabilities of neutrophil and platelet recovery, acute and chronic GVHD, OS, NRM for HSCT recipients with diabetes and HSCT recipients without diabetes were estimated by the Kaplan–Meier method. Curves among the two groups were compared by the log rank test in a univariate analysis.

Multivariate analysis was performed to assess the association between confounders and the stated transplant outcomes. Confounders included sex, age, primary diagnosis requiring transplantation, post-transplant FPG, and body mass index (BMI). The Cox proportional hazard regression model was applied for multivariate analysis. Data of all recipients were analyzed using a backward stepwise method in Cox regression analysis. Post-transplantation FPG was first modeled as a time-dependent variable.

All statistical analysis was performed by STATA software version 11 (StataCorp, College Station, TX) and a p value <0.05 was considered significant.

Results

Patients

During the study time period (March 1991 up to July 2011), 34 HSCT recipients with diabetes were identified who fulfilled the study inclusion criteria. Data were compared with a group of 71 HSCT recipients without diabetes.

In terms of condition requiring transplantation, 5 (14.7%) patients in the diabetes group had acute myelogenous leukemia (AML), 2 (5.9%) acute lymphoblastic leukemia (ALL), 3 (8.8%) chronic lymphocytic leukemia (CML), 12 (35.3%) multiple myeloma, 4 (11.8%) beta thalassemia major, 6 (17.6%) non-Hodgkin's lymphoma (NHL), 1 (2.9%) Hodgkin's disease (HD), and 1 (2.9%) aplastic anemia. Similarly, in the non-diabetic group, 16 (22.5%) patients had AML, 7 (9.9%) CML, 24 (33.8%) multiple myeloma, 7 (9.9%) beta thalassemia major, 8 (11.3%) NHD, 5 (7%) HD, 2 (2.8%) aplastic anemia, and 2 (2.8%) myelodysplastic syndrome. Baseline characteristics of study patients are summarized in Table 1.

Mean (SD) FPG of study participants after HSCT was 9.54 (3.71) mmol/L in the diabetic group and 6.58 (1.34) mmol/L in

Table 1. Patients' characteristics at baseline.

	Diabetes	No diabetes
FPG (mmol/L)[a]	8 (4.39)	4.88 (1.75)**
BW (kg)[a]	71.63 (14.86)	65.06 (11.75)*
BMI (kg/m^2)[a]	26.80 (5.75)	24.32 (3.86)*
Age (year)[a]	43.70 (13.90)	43.15 (13.57)
CD_{34} cell ($\times 10^6$/kg recipient)[b]	18.76 (59.66)	10.06 (33.18)
Total MNC ($\times 10^8$/kg recipient)[b]	9.60 (13.46)	7.36 (3.63)
Sex (*N*, %)		
Male	20	40
Female	14	31
Transplantation type (*N*, %)		
Autologue	22	44
Allogeneic	12	27

FPG, fasting plasma glucose; BW, body weight; BMI, body mass index; MNC, mononucleated cell.

Data are presented as mean (SD) for FBS, BW, BMI, age, CD_{34} cell, and total MNC. Data are presented as *N* (%) for sex and transplantation type. Mean FPG, BW, and BMI of recipients are reported before initiation of conditioning regimen.

[a]*p* Values are given for the comparison of mean difference between diabetes and non-diabetes groups using independent sample *t*-test.

[b]*p* Values are given for the comparison of difference between diabetes and non-diabetes groups using the Mann–Whitney test.

*p Value of <0.05. **p Value of <0.001.

Table 2. Transplantation outcomes in patients with and without diabetes.

	Diabetes ($n=34$)	No-diabetes ($n=71$)
Length of hospital stay, mean (SD), days	17.58 (10.85)	18.14 (5.34)
Neutrophil engraftment[a] (%)	85.3	93
Platelet engraftment[a] (%)	44.1	63.4
Febrile neutropenia[a] (%)	97.1	93
Acute GVHD[a] (%)	20.6	16.9
Chronic GVHD[b] (%)	8.8	14.1
Relapse/recurrence[b] (%)	14.7	26.8
Overall survival[b] (%)	79.4	88.7
NRM[b] (%)	17.6	5.6

GVHD, graft-versus-host disease; NRM, non-relapse mortality. None of the variables were significantly different between the two groups.

[a]Incidence of neutrophil engraftment, platelet engraftment, febrile neutropenia, and acute GVHD were assessed during hospitalization calculated from day of stem cell infusion to discharge.

[b]Incidence of chronic GVHD, survival, relapse, and NRM were reported and compared for the median time of patient follow-up.

the control group ($p<0.001$). The median (IQR) duration of follow-up for survived patients was 1338 d (821–1913) in the diabetes group and 1450 d (805–1899) in the control group.

Comparison of study endpoints between HSCT recipients with diabetes and HSCT recipients without diabetes

As shown in Table 2, there was no difference in mean length of hospital stay as well as occurrence of the other primary and secondary outcomes between the two groups.

Kaplan–Meier estimations of study endpoints between HSCT recipients with diabetes and HSCT recipients without diabetes

Median times for neutrophil and platelet engraftment, acute and chronic GVHD as well as median time to febrile neutropenia, primary disease relapse/recurrence, and OS are depicted in Table 3. There was no difference between recipients with diabetes and the control arm.

Multivariate analysis to detect prognostic factors associated with study outcomes

Risk factors associated with each outcome is demonstrated in Table 4. Multivariate analysis demonstrated that having diabetes before HSCT significantly decreased overall survival (hazard ratio 0.51, 95% confidence interval 0.27–0.97, *p* value: 0.04). However, pre-transplantation diagnosis of diabetes showed no association with other study outcomes. Primary diagnosis requiring transplantation independently predicted hematopoietic recovery, febrile neutropenia, and OS. The age of HSCT recipients demonstrated to be a prognostic factor for acute GVHD whereas BMI of recipients was found to have a near significant relationship for chronic GVHD (hazard ratio 1.41, 95% confidence interval 0.99–2.02, *p* value: 0.05).

Discussion

To the authors' knowledge, this is the first study specifically aimed to evaluate the outcomes of HSCT in patients with diabetes. Based on the results of this study, a known diagnosis of diabetes mellitus pre-transplantation was associated with decreased OS; however, it did not affect other studied outcomes. In our work, we observed that having diabetes affects survival with a hazard ratio of 0.51. This corresponds to 49% increase in risk of death in diabetic hematopoietic recipients when compared with non-diabetic recipients. Of note, we observed this relation after adjusting for important covariates including post-transplantation FPG. Thus, results of this study suggest that preexisting diabetes mellitus could be regarded as a new risk factor for at least one transplantation outcome.

In corroboration with our results, Pidala et al. evaluated the impact of dysglycemia following glucocorticoid therapy in the setting of acute GVHD in a group of patients undergoing HSCT in a retrospective manner. The study population incorporated recipients with and without prior diagnosis of diabetes. The study demonstrated that post-transplant maximum and average glucose values would predict OS and having diabetes mellitus at baseline is associated with higher maximum and average blood glucose levels. The study suggested diabetic recipients as a high risk group for hematopoietic transplantation who deserve particular attention. However, Pidala et al. trial was not designed to investigate the specific impact of prior diabetes on outcomes (7). The presence of diabetes mellitus has also been proposed to be an important determinant of morbidity in autologous HSCT. In a case series, Schouten et al. reported outcomes of eight patients with type 2 diabetes mellitus or an impaired glucose tolerance undergoing autologous bone marrow transplantation (21). In the study, six recipients suffered life-threatening infection, three developed acute kinder injury, four liver injuries, and one congestive heart failure. Likewise a worse OS has been reported in cancer patients with diabetes compared with their counterparts without diabetes (22).

The mechanisms underlying the negative influence of diabetes on survival remain to be elucidated.

Table 3. Probabilities of transplant outcomes.

	Diabetes ($n = 34$)	No-diabetes ($n = 71$)
Time to neutrophil engraftment, median (IQR), days	16 (10–20)	11 (10–14)
Time to platelet engraftment, median (IQR), days	21 (13–16)	15 (13–28)
Time to febrile neutropenia, median (IQR), days	5 (4–8)	6 (5–8)
Time to aGVHD, median (IQR), days	45 (12–100)	100 (13–100)
Time to cGVHD, median (IQR), days	290 (84–1415)	850 (146–1610)
Time to relapse/recurrence, median (IQR), days	1285 (115–1551)	1155 (256–1650)
Time to overall survival, median (IQR), days	1492 (1247–2158)	1500 (1140–1950)

IQR, inter-quartile range; aGVHD, acute graft-versus-host disease; cGVHD, chronic graft-versus-host disease. None of the variables were significantly different between the two groups.

Table 4. Predictive factors related to transplantation outcomes.

Outcomes and variables	Hazard ratio (95% confidence interval)
Neutrophil engraftment	
Disease	
ALL/AML	Reference
Thalassemia	0.359 (0.138–0.932)*
NHD	0.308 (0.119–0.800)*
Platelet engraftment	
Disease	
ALL/AML	Reference
Thalassemia	0.294 (0.091–0.949)*
NHD	0.081 (0.010–0.640)*
Overall survival	
Diabetes	
No	Reference
Yes	0.515 (0.273–0.972)*
Disease	
ALL/AML	Reference
MM	4.149 (1.737–9.914)*
NHD	4.062 (1.360–12.129)*

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; NHD, non-Hodgkin's disease; MM, multiple myeloma. Data are analyzed using a backward stepwise method in Cox regression multivariate analysis. *p Value < 0.05.

Long-term diabetes has been shown to impair mobilization and function of hematopoietic progenitor cells in mice (23,24). The clinical impact of these finding needs further research.

In our study, however, a known diagnosis of diabetes mellitus pre-transplantation did not affect granulocyte and platelet recovery, acute and chronic GVHD, length of hospital stay, primary disease recurrence, febrile neutropenia, and NRM. This result may be attributed to the small sample size of study population. Additionally, this result may be interpreted with the mechanisms underlying the ''diabetes paradox'' theory. This theory delineates that diabetes mellitus is not independently associated with decreased mortality in critically ill patients (25).

Regarding the effect of the condition requiring transplantation, we observed that NHD independently predicted hematopoietic recovery as well as OS and thalassemia affected hematopoietic recovery. It has been shown that adult thalassemia patients over 17 years undergoing HSCT from HLA identical siblings have higher transplantation related mortality (TRM), a lower OS and thalassemia free survival (TFS) compared with younger counterparts undergoing HSCT (26–28). In the present work, however, we observed that adult patients with thalassemia have inferior rates of hematopoietic recovery.

Baseline BMI of HSCT recipients has been reported to be a potential outcome predictor following allogeneic HSCT in leukemic patients (29). In the present trial, higher BMI had a near significant association with increased risk of chronic GVHD. This finding is consistent with Fuji et al. (30) illuminating an association between obesity and GVHD.

Not surprisingly, diabetic recipients had significantly higher fasting plasma glucose levels in the post-transplantation period compared with the control arm; mean (SD) FPG of 9.54 (3.71) mmol/L versus 6.58 (1.34) mmol/L (p value < 0.001), respectively. There is growing evidence on the role of hyperglycemia in the post-transplantation period on the outcomes of transplantation (3–6).

This study has a number of limitations. This research had a retrospective nature. Also, it had the limited sample of diabetic patients. However, this sample consisted of all diabetic patients undergoing HSCT in our institution. Data on glycosylated hemoglobin A_{1c} (HbA_{1c}) were not available. Additionally, information on duration of diabetes, development of diabetes complications, type of anti-diabetes medications, and Karnofsky performance status of recipients were unavailable. Moreover, heterogeneous population of malignant and non-malignant diseases in this study could have influenced the results. Finally, incidence of neutrophil engraftment, platelet engraftment, febrile neutropenia, and acute GVHD were assessed within hospitalization time.

Conclusion

Patients with diabetes mellitus undergoing HSCT may have inferior transplantation outcomes compared with recipients without diabetes mellitus. Considering the rapidly growing population of diabetes (31), studies on the consequences of diabetes in the setting of hematopoietic transplantation are mandatory.

Declaration of interest

None to declare. This study was a Pharm.D. thesis supported by Tehran University of Medical Sciences (TUMS).

References

1. Karnchanasorn R, Malamug LR, Jin R, et al. Hyperglycemia is associated with prolonged hospital stay but has no impact on engraftment after autologous hematopoietic stem cell transplantation. Endocr Pract 2012;22:1–30.

2. Marvin MR, Morton V. Glycemic control and organ transplantation. J Diabetes Sci Technol 2009;3:1365–72.
3. Sheean PM, Braunschweig C, Rich E. The incidence of hyperglycemia in hematopietic stem cell transplant recipients receiving total parenteral nutrition: a pilot study. J Am Diet Assoc 2004;104: 1352–60.
4. Sheean PM, Freels SA, Scott Helton W, Braunschweig CA. Adverse clinical consequences of hyperglycemia from total parenteral nutrition exposure during hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 2006;12:656–64.
5. Fuji S, Kim SW, Mori SI, et al. Hyperglycemia during the neutropenic period is associated with a poor outcome in patients undergoing myeloablative allogeneic hematopoietic stem cell transplantation. Transplantation 2007;84:814–20.
6. Garg R, Bhutani H, Alyea E, Pendergrass M. Hyperglycemia and length of stay in patients hospitalized for bone marrow transplantation. Diabetes Care 2007;30:993–4.
7. Pidala J, Kim J, Kharfan-Dabaja MA, et al. Dysglycemia following glucocorticoid therapy for acute graft-versus-host disease adversely affects transplantation outcomes. Biol Blood Marrow Transplant 2011;17:239–48.
8. Griffith ML, Jagasia MH, Misfeldt AA, et al. Pretransplantation c-peptide level predicts early posttransplantation diabetes mellitus and has an impact on survival after allogeneic stem cell transplantation. Biol Blood Marrow Transplant 2011;17:86–92.
9. Chow EJ, Mueller BA, Baker KS, et al. Cardiovascular hospitalizations and mortality among recipients of hematopoietic stem cell transplantation. Ann Intern Med 2011;155:21–32.
10. Munakata W, Sawada T, Kobayashi T, et al. Mortality and medical morbidity beyond 2 years after allogeneic hematopoietic stem cell transplantation: experience at a single institution. Int J Hematol 2011;93:517–22.
11. Griffith ML, Jagasia M, Jagasia SM. Diabetes mellitus after hematopoietic stem cell transplantation. Endocr Pract 2010;16: 699–706.
12. Hammer MJ, Casper C, Gooley TA, et al. The contribution of malglycemia to mortality among allogeneic hematopoietic cell transplant recipients. Biol Blood Marrow Transplant 2009;15: 344–51.
13. Saraiva J, Sola E, Prieto D, Antunes MJ. Diabetes as an outcome predictor after heart transplantation. Interact CardioVasc Thorac Surg 2011;13:499–504.
14. Yoo HY, Thuluvath PJ. The effect of insulin-dependent diabetes mellitus on outcome of liver transplantation. Transplantation 2002; 15:1007–12.
15. Shields PL, Tang H, Neuberger JM, et al. Poor outcome in patients with diabetes mellitus undergoing liver transplantation. Transplantation 1999;68:530–5.
16. Ling Q, Xu X, Wei Q, et al. Impact of preexisting diabetes mellitus on outcome after liver transplantation in patients with hepatitis B virus-related liver disease. Dig Dis Sci 2011;56: 889–93.
17. John PR, Thuluvath PJ. Outcome of liver transplantation in patients with diabetes mellitus: a case-control study. Hepatology 2001;34: 889–95.
18. Nampoory MR, Johny KV, Costandi JN, et al. Inferior long-term outcome of renal transplantation in patients with diabetes mellitus. Med Princ Pract 2002;11:29–34.
19. Hofer M, Schmid C, Benden C, et al. Diabetes mellitus and survival in cystic fibrosis patients after lung transplantation. J Cyst Fibros 2012;11:131–6.
20. American Diabetes Association. Standards of medical care in diabetes-2010. Diabetes Care 2010;33:S11–61.
21. Schouten HC, Maragos D, Vose J, Armitage JO. Diabetes mellitus or an impaired glucose tolerance as a potential complicating factor in patients treated with high-dose therapy and autologous bone marrow transplantation. Bone Marrow Transplant 1990;6:333–5.
22. van de Poll-Franse LV, Houterman S, Janssen-Heijnen MLG, et al. Less aggressive treatment and worse overall survival in cancer patients with diabetes: a large population based analysis. Int J Cancer 2007;120:1986–92.
23. Ferraro F, Lymperi S, Mendez-Ferrer S, et al. Diabetes impairs hematopoietic stem cell mobilization by altering niche function. Sci Transl Med 2011;12:104ra101.
24. Orlandi A, Chavakis E, Seeger F, et al. Long-term diabetes impairs repopulation of hematopoietic progenitor cells and dysregulates the cytokine expression in the bone marrow microenvironment in mice. Basic Res Cardiol 2010;105:703–12.
25. Krinsley JS, Fisher M. The diabetes paradox: diabetes is not independently associated with mortality in critically ill patients. Hosp Pract 2012;40:31–5.
26. Lucarelli G, Galimberti M, Polchi P, et al. Bone marrow transplantation in thalassemia. Hematol Oncol Clin N Am 1991; 5:549–56.
27. Lucarelli G, Galimberti M, Polchi P, et al. Bone marrow transplantation in adult thalassemia. Blood 1992;80:1603–7.
28. Lucarelli G, Clift RA, Galimberti M, et al. Bone marrow transplantation in adult thalassemic patients. Blood 1999;93: 1164–7.
29. Hadjibabaie M, Tabeefar H, Alimoghaddam K, et al. The relationship between body mass index and outcomes in leukemic patients undergoing allogeneic hematopoietic stem cell transplantation. Clin Transplant 2012;26:149–55.
30. Fuji S, Kim SW, Yoshimura K, et al. Possible association between obesity and posttransplantation complications including infectious diseases and acute graft-versus-host disease. Biol Blood Marrow Transplant 2009;15:73–82.
31. Wild S, Roglic GM, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047–53.