

Prevalence and Distribution of Diabetes Mellitus in a Maximum Care Hospital: Urgent Need for HbA_{1c}-Screening

Authors

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ABSTRACT

Objective Diabetes mellitus affects almost one in 10 individuals in Germany. So far, little is known about the diabetes prevalence in maximum care hospitals. We assessed the diabetes prevalence, proportion of undiagnosed cases, the effectiveness of diabetes screening in a university hospital, the consequences for hospital stay and acquired complications.

Research Design and Methods Over a 4 week period we determined HbA_{1c} from 3 733 adult patients which were hospitalized at the university hospital of Tuebingen and had an available blood sample. Diabetes diagnosis was defined as HbA_{1c} ≥ 6.5 % and/or previously documented diabetes diagnosis, prediabetes was defined as HbA_{1c} ≥ 5.7 % and < 6.5 % without history of previous diabetes.

Results 23.68 % of the patients had prediabetes and 22.15 % had diabetes with a high variation between the specialised departments (range 5–43 %). The rate of unknown diabetes was 3.7 %, the number needed to screen was 17 in patients older than 50 years. Patients with diabetes had a prolonged hospital stay compared to the mean length of stay for their diagnosis related group (diabetes: 1.47 ± 0.24 days; no diabetes: –0.18 ± 0.13 days, $p = 0.0133$). The prevalence of hospital acquired complications was higher in diabetic patients (diabetes: 197 of 630; no diabetes: 447 of 2 459, $p < 0.0001$).

Conclusions Every fourth patient in the university hospital had diabetes and every second had either prediabetes or diabetes. It is also worthwhile to screen for unknown diabetes in patients over the age of 50. The high prevalence and negative consequences of diabetes require screening and intensified specialized diabetes treatment in hospitals.

* Andreas Fritsche and Andreas Peter contributed equally

Introduction

Diabetes mellitus with its impacts on health, the healthcare system and healthcare expenses of individuals represents a serious global health burden [1]. A worldwide trend analysis of diabetes prevalence, which included 4 372 000 adults from 200 countries, showed a gender-independent increase of age-standardized diabetes prevalence between 1980 and 2014. Currently, the worldwide age-standardized adult diabetes prevalence is 7.9 % for women and 9.0 % for men [2]. Diabetes mellitus is also a major health risk in German adults with a known prevalence between 7.2 % and 9.9 % and a further 2 % to 7 % of unknown cases [3–5]. Taking into account the drastic increase of overweight and obesity as well as the steadily ageing population and declining physical activity, a further increase in diabetes incidence is very likely.

The direct and total costs of diabetes caused by its accompanying and secondary diseases in Germany are estimated to be 21 and 48 billion Euros per year respectively (2009) [6]. Patients with diabetes are more often admitted to hospitals and the intensive care unit (ICU) and therefore require more infection management than people without diabetes [7–9]. Unknown/undiagnosed diabetes is an additional risk factor for myocardial infarction and mortality, especially in ICU patients [9, 10]. Furthermore, diabetic patients do not only have a higher risk of in-hospital mortality when suffering from an acute myocardial infarction [11], but also have a longer hospital stay than those without diabetes [11–12].

The availability of the correct diagnosis of diabetes mellitus is crucial for adequate clinical treatment in general. The aim of this study was to answer the following questions. What is the diabetes prevalence in a university hospital of maximum care and how the disease is distributed in the different departments of the hospital and what are the consequences of diabetes for the length of hospital stay and acquired complications? Furthermore, we asked how common is unknown/undiagnosed diabetes? These lead to the main question: what is the number needed to screen to detect diabetes with a standardized HbA_{1c}-screening?

Research Design and Methods

Study population and design

This non-interventional cross-sectional study was performed during a 4 week period (Feb 16th–Mar 16th 2016). It included all in-patient adults (age > 18), for which blood testing including an EDTA-blood sample during their clinical stay was required and diagnosis related groups (DRG) were applied for billing (► **Fig. 1**). HbA_{1c} was routinely determined once from each enrolled patient. The results of these tests were not immediately reported to the physician and therefore did not influence the regular diagnostic procedures or DRG classification. However, in case of significantly elevated HbA_{1c} the attending physician was informed. The study was performed with the approval of the local ethics committee, in accordance with national law and in accordance with the declaration of Helsinki of 1975 (in the current, revised version).

Analytical procedures

HbA_{1c} measurements were performed in the central laboratory of the university hospital of Tuebingen using the Tosoh glycohemoglobin analyzer HLC-723G8 (Tosoh Bioscience GmbH, Griesheim, Germany) from fresh residual EDTA blood samples. The laboratory has an accreditation according to DIN EN ISO 15189 and internal quality controls were always within the allowed limits. The coefficient of variation during the study was 1.42 % at 5.01 % HbA_{1c} and 0.89 % at 9.64 % HbA_{1c}. External quality controls are performed 4 times per year and the values were well within the allowed ranges.

Diagnosis of diabetes mellitus

In the present study, patients were categorized after HbA_{1c} measurement: diabetes mellitus (HbA_{1c} ≥ 6.5 %), prediabetes (5.7 % ≤ HbA_{1c} < 6.5 %) and no diabetes mellitus (HbA_{1c} < 5.7 %) as recommended in the guidelines and practice recommendations of the German and the American Diabetes Association [13–14].

The use of HbA_{1c} as the screening tool and the application of the intermediate HbA_{1c}-range as an appropriate measure to identify individuals with prediabetes has been shown in previous studies [15–17]. We further subgrouped the patients into those who had a regular request for HbA_{1c} measurements by the attending clinicians and those who only had this measurement done as part of the screening protocol for this study. Additionally, all patients who were previously diagnosed with diabetes and had any diabetes documentation in their billing information were defined as known individuals with diabetes. This was done using the International Classification of Diseases (ICD) codes in the 10th revision, German Modification: E10.- to E14.- and O24.-.

The overall prevalence of non-diabetes, prediabetes and diabetes was determined combining the HbA_{1c} measurements and the information about previous diabetes diagnosis in the billing information using the following definitions:

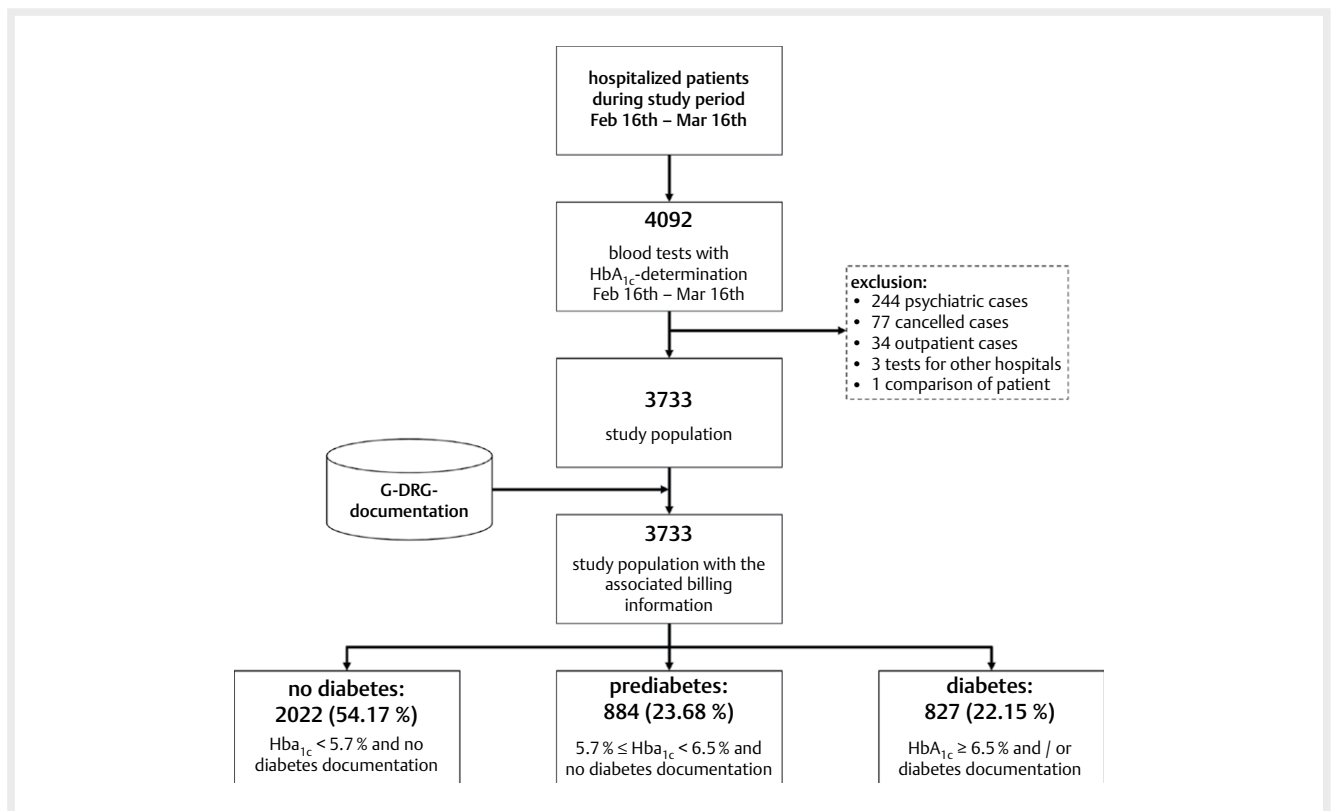
no diabetes: HbA_{1c} < 5.7 % and no diabetes documentation

prediabetes: 5.7 % ≤ HbA_{1c} < 6.5 % and no diabetes documentation

diabetes: HbA_{1c} ≥ 6.5 % and or any diabetes documentation

Consideration of length of hospital stay

The length of hospital stay (LOS) strongly depends on the primary disease, and on the reason for hospitalization. The German compensation system classifies all hospital stays in Diagnosis Related Groups (DRGs), taking this dependency into account. For each DRG there is a corresponding LOS with an associated mean length of stay (mLOS). In Germany the corresponding LOS of each DRG is also limited by the lower duration limit of length of stay (lLOS) and the upper duration limit of length of stay (uLOS). [18] The duration limits are set to identify abnormally short or long-term in-patient stays. This enables the classification of patients into 3 groups: intermediate-term in-patients (LOS between lLOS and uLOS), short-term in-patients (LOS < lLOS) and long-term in-patients (LOS > uLOS). In order to assess one or more influencing factors on the LOS regardless of the primary diagnosis, the deviation in days between the real LOS of a case and the respective mLOS of the corresponding DRG (dLOS = real LOS - mLOS) have been considered.



► **Fig. 1** Flow chart and distribution of the study population.

Evaluation of the occurrence of complication during hospitalization

For the evaluation of the occurrence of complications during the hospital stay the billing information was re-used. All patients with at least one of the following ICD-10 code were defined as patient who suffered complications during hospitalization: E89.-, G97.-, H59.-, H95.-, I97.-, J95.-, K91.-, L89.-, M96.-, N99.-, T80-T88, U69.00!, U69.10!

Statistics

The significance level for all analyses was set at $p \leq 0.05$. The data was analyzed with the statistical software SAS (SAS Institute Inc., Cary, NC, USA, version 9.4).

The normal distribution of the continuous variables was tested using the Kolmogorov–Smirnov test. The potential correlations of the diabetes status with the dLOS and the occurrence of a complication during hospitalization were tested univariately using the non-parametric Mann-Whitney-U test and Fisher's exact test.

The influence of the diabetes status on the dLOS, which was adjusted for further risk factors, was determined by multiple linear regression. The regardless predictors were tested for multi-collinearity. Dummy variables were created for all nominal or ordinal scaled potential influencing factors.

Results

Clinical characteristics of the study population

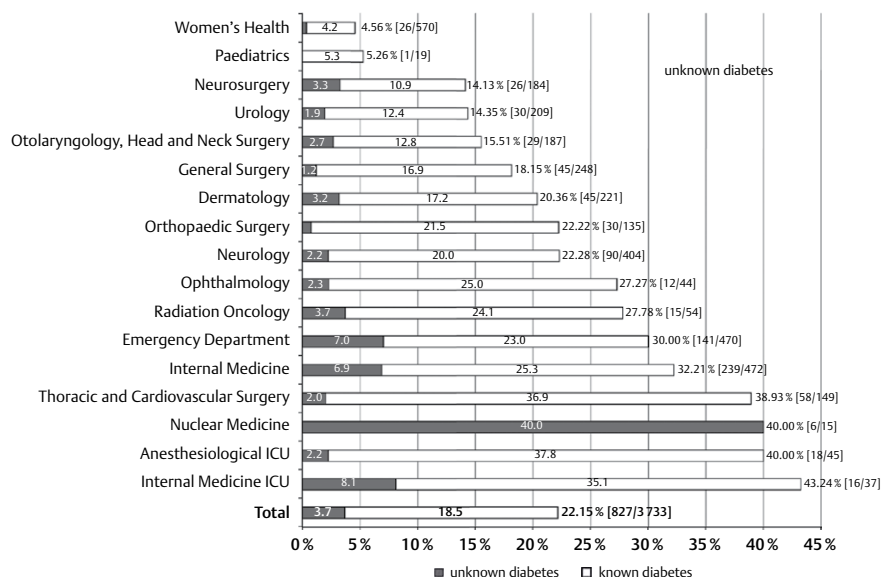
On the day of admission the study participants were aged between 18 to 99 (mean age: 59.13 ± 18.40 years). 1 869 (50.07 %) of them were female and 1 864 (49.93 %) male. The mean length of stay was 8.33 days (± 12.80 days), and 644 (17.25 %) developed at least one complication during hospitalization.

Prevalence of diabetes mellitus

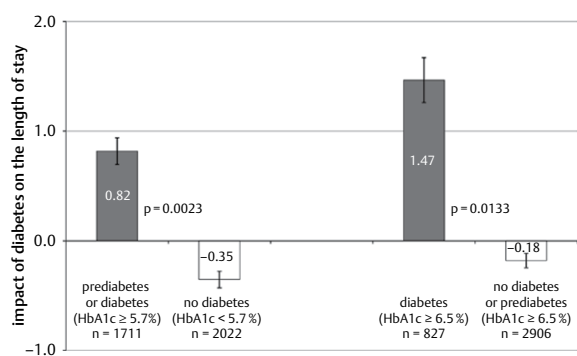
Of the 3 733 patients, 54.17 % had no diabetes, 23.68 % had prediabetes and 22.15 % had diabetes (see ► **Fig. 1**). The prevalence of diabetes according to the departments where the patients were treated in the university hospital is shown in ► **Fig. 2**. The prevalence showed considerable variation with a maximal prevalence in intensive care units of more than 40 % and a minimal prevalence in the women's health department with nearly 5 %. The prevalence of unknown/undiagnosed diabetes was overall 3.67 %. The prevalence of diabetes according to the HbA_{1c} measurements alone was considerable lower than the overall prevalence including previous diagnosis and HbA_{1c} measurement. 545 patients (14.60 %) had diabetes according to HbA_{1c} measurement (HbA_{1c} ≥ 6.5 %) alone.

Outcome of the HbA_{1c}-screening

From patients hospitalized during the study period 63.16 % had requests for a blood test including an EDTA-blood sample, whereas 36.84 % had no such sample and could therefore not be included



► **Fig. 2** Prevalence of diabetes mellitus in a maximum care hospital; grey bars: unknown diabetes; white bars: known diabetes.



► **Fig. 3** Impact of diabetes on the length of stay in the hospital. Length of stay is represented by the deviation in days between the real length of stay of a case and the respective mean length of stay of the corresponding diagnosis related group.

in the routine HbA_{1c} screening protocol. The percentage of the hospitalized patients with a routine EDTA-blood draw who had a HbA_{1c} measurement requested by the attending physician was 15.08 % (563 of 3733). 90 % of the patients without diabetes had no request for a HbA_{1c} measurement. Of those patients with known diabetes only 34 % had an actively requested HbA_{1c} during their stay in the hospital.

Influences of diabetes mellitus

The univariate consideration of the correlation between diabetes status and dLOS showed a significant longer stay for patients with diabetes or prediabetes (► **Fig. 3**). Within the group of long-term in-patients the difference between mean length of stay and the actual duration of stay of patients with diabetes was significantly

($p = 0.0232$) higher than with patients without diabetes (diabetes: 22.53 ± 22.24 vs. no diabetes: 16.79 ± 14.35 days). A multivariate analysis also showed a significant influence of the diabetes status on dLOS. The deviation to mLOS of the corresponding DRG increased by 1.101 days when a patient had diabetes and 5.141 days for each additional patient with a complication occurring during hospitalization. Age, gender and death had no significant influence on the dLOS (see ► **Table 1**).

Complications were significantly ($p < 0.0001$) more frequent among patients with diabetes ($\text{HbA}_{1c} \geq 6.5\%$ or any diabetes documentation) or with prediabetes and diabetes ($\text{HbA}_{1c} \geq 5.7\%$ or any diabetes documentation). The determined relative risk was 1.50 (CI: [1.31; 1.72]) for patients with diabetes. Patients with prediabetes and diabetes have a relative risk of 1.24 (CI: [1.14; 1.34]) (see ► **Fig. 4**).

Number needed to screen

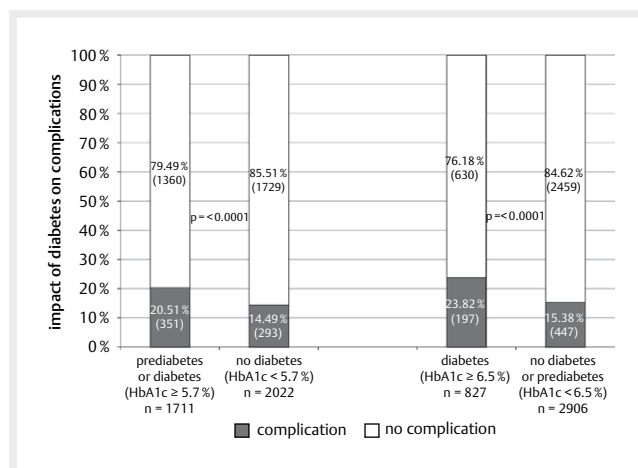
The number needed to screen (NNS) to detect unknown/undiagnosed diabetes depends on the patient age limit from which is screened by default. With increasing limits of the patients age, the NNS decreases. The overall NNS was 23.14. When considering various trendlines of NNS, it is noticeable that the slope of the trendlines from an age limit of minimum 50 years and above came to a nearly constant flat level. By implementation the screening measurement standardized at the age of 50 years and above the NNS was 17.22. The NNS for the different patient age limits are shown in ► **Fig. 5**.

Conclusions

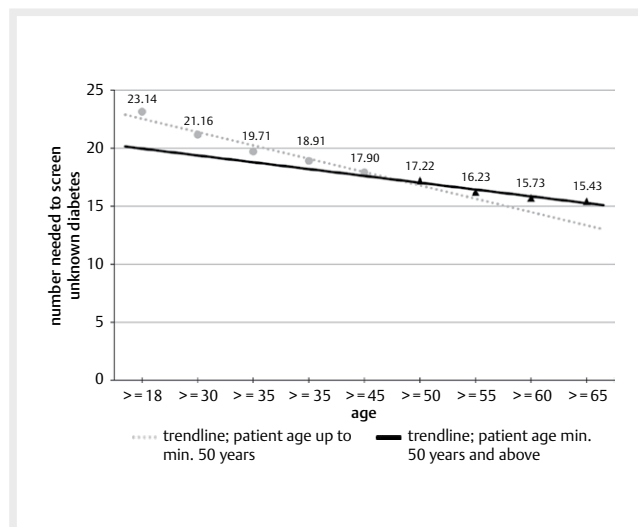
These findings demonstrate convincingly that a substantial proportion of hospitalized patients in a maximum care hospital had diabetes (22.15 %) or prediabetes (23.68 %) and a relevant number of indi-

► **Table 1** Multivariate influence of diabetes status on deviation in days between the real length of stay in hospital of a patient and the respective mean length of stay of the corresponding diagnosis related group.

predictor	parameter estimate	SE	95% CI	p-value
intercept	-1.572	0.456	[-2.466; -0.678]	0.0006
diabetes status * (ref.: no diabetes)	1.101	0.335	[0.444; 1.757]	0.0010
complication (ref.: no complication)	5.141	0.356	[4.444; 5.840]	<.0001
age	0.009	0.008	[-0.006; 0.024]	0.2382
gender (ref.: female)	0.211	0.211	[-0.322; 0.744]	0.4376
death (ref.: normal discharge or relocation to other healthcare facility)	-0.754	0.944	[-2.605; 1.097]	0.4246
* diabetes: HbA _{1c} ≥ 6.5 % and/or diabetes documentation				
no diabetes: HbA _{1c} < 6.5 % and no diabetes documentation				
R ² = 0.0609; adjusted R ² = 0.0597; sum of squares SS = 263 483; p < 0.0001; N = 3 733;				
CI confidence interval; SE standard error				



► **Fig. 4** Impact of diabetes on complications; grey bars: percentage of patients with acquired complications, white bars: percentage of patients with no acquired complications.



► **Fig. 5** Number needed to screen unknown diabetes; Gray dotted line: trendline patient age up to min. 50 years, black line: trendline patient age min. 50 years and above.

viduals (3.67 %) had not yet been diagnosed with the disease. For our university hospital, this implies that about 13 290 of our 60 000 adult inpatients per year have diabetes, and 2 202 of these patients have unknown/undiagnosed diabetes. Additionally 14 208 adult patients per year can be expected to have prediabetes. The so far very rarely published data about diabetes prevalence in hospitals is enhanced by our results. Furthermore, we provide knowledge about the distributions of diabetes prevalence stratified by the departments where the patients were treated in a hospital of maximum care.

The negative effects of a prevalent diabetes mellitus on the occurrence of complications are in line with published data [19]. In addition, the results show that the occurrence of complications is already significantly increased in patients with prediabetes. The evaluation of the adjusted influence of diabetes on length of hospital stay show that patients with diabetes stay on average 1.1 days longer than patients with no diabetes or prediabetes. This significant impact of diabetes on the length of hospital stay is confirmed by other studies [11, 20]. A previous study showed that the activation and subsequent intervention of a diabetes care team diminishes the average length of stay of patients with diabetes [20]. In our hospital which is certified according to the German Diabetes Association (DDG) all patients with known diabetes were given access to a diabetes care team. It is therefore remarkable that the effect of diabetes on the length of hospital stay was nonetheless significant [20]. This points to the necessity for continuing education in all medical departments in a maximum care hospital to screen for diabetes and promptly call and involve the diabetes team in the treatment of patients with diabetes.

Evaluation of the HbA_{1c}-screening

The percentage of hospitalized patients with a routine blood draw who had a HbA_{1c} measurement requested by the attending physician was 15.08 %. As a consequence of this, 90 % of the patients without diabetes had no HbA_{1c} measurement requested by the attending physician. Importantly, only 34 % of patients with known diabetes had an actively requested HbA_{1c} measurement after admission to the hospital. This number is far too low, as an actual HbA_{1c} level may be important for the planning of therapeutic interventions on the patient.

The evaluation of the different NNS values showed an appropriate benefit from a HbA_{1c} measurement from patients above the age of 50 compared to the expenditure of HbA_{1c} testing. Within the group of patients aged over 50, 17.22 HbA_{1c} measurements must be performed to detect one patient with unknown diabetes. The reimbursement for the laboratory to determine HbA_{1c} in the German public health system is 4 Euros per HbA_{1c} measurement [21]. According to this, diagnosing a patient with unknown diabetes costs on average 68.88 Euros. In the United States of America, the determination of HbA_{1c} is reimbursed using current procedural terminology (cpt). The cpt codes for HbA_{1c} are 83036 and 83036QW and their Medicare reimbursement is 13.42 Dollars in almost every state [22]. According to this, identifying a patient with unknown diabetes costs on average 231.09 Dollars.

It is self-evident that an appropriate therapy for a hospitalized patient with diabetes must be given to the patient as early as possible during the hospital stay. This is especially important as the length of hospital stay is decreasing continuously in Germany. Thus the mLOS has fallen in the past 20 years from 11.5 days and in the last 10 years from 8.7 days to an average of 7.4 days in 2015 [23]. A benefit of the standardized screening is the additionally available HbA_{1c} values which enables an adaptation and intensification of the therapy also for patients with known diabetes.

Limitations and strengths

In this screening approach, only those patients whose blood was actually tested during their hospital stay were included. There were 36.84 % patients without a blood test including EDTA-blood sample. This percentage can be explained by the fact that not all departments are using the possibility of a routine blood test. In addition to the HbA_{1c} measurements, that were performed with a highly reliable chromatographic laboratory method [24, 25], we used data from the billing information to detect diabetes. In the billing information, a known diabetes might not be documented inadvertently due to incomplete information from the general practitioner or the patient. This may lead to a slight underestimation of diabetes prevalence.

Finally, we only used HbA_{1c} and omitted glucose levels for screening. Previous studies have shown that the sensitivity of HbA_{1c} screening to detect diabetic patients is lower than the one of the time consuming OGTT [15]. However, only the independence of nutrient ingestion and the low pre-analytical requirements of HbA_{1c} enable us to perform this kind of study in the routine setting of a university hospital trying to include almost all patients [26]. The inclusion of an additional OGTT may have resulted in a higher diabetes prevalence in the tested group, but practically limits the number of patients participating in the screening, which would result in a lower number of newly detected subjects with diabetes. HbA_{1c} is therefore an accepted screening tool for diabetes, which is reflected by the ADA guidelines for diabetes screening [14]. HbA_{1c} reflects long-term hyperglycemia over the preceding 2–3 months and is a proven measure of diabetes-related complications. Although HbA_{1c} may be altered by factors other than glucose, (e. g., change in erythrocyte life span, anemia, uremia, selected hemoglobinopathies and also ethnicity) [27–31] it still is a useful and practical tool for diabetes screening for the vast majority of in-patients HbA_{1c} [27].

Conclusion

The results of the present study show that nearly every fourth adult in-patient has diabetes and every second has prediabetes or diabetes. The diagnosis of diabetes is associated with prolonged hospital stay and a significantly increased prevalence of acquired complications during the hospital stay. That emphasizes the urgent need for physicians and clinical institutions to be aware of diabetes mellitus in a large university hospital, with its special spectrum of patients. High prevalence and negative consequences of diabetes diagnosis require diabetes screening and an early additionally intensified specialized diabetes treatment in hospitals with maximum care.

Author contributions

J.K., A.F. & A.P.: performed data acquisition an analysis, statistical analysis, literature search and wrote the manuscript. J.K.: created the figures. M.K. & A.P.: performed laboratory measurements. M.A., M.B. & H.-U.H.: revised the manuscript. A.F., A.P., H.S. & J.K.: developed the design of the study.

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Conflict of Interest

J. K. reports an doctoral scholarship from B. Braun Melsungen AG, during the conduct of the study and outside the submitted work. No other potential conflicts of interest relevant to this article were reported. All coauthors approved the final version to be published. A. F. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. None of the material contained in this paper has been published, nor is it under consideration for publication elsewhere.

One sentence summary: Every fourth hospitalized patient in the study had diabetes which causes more complications and an increasing length of hospital stay. This shows the requirement of a screening and an intensified specialized diabetes treatment.

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