

CHAPTER 1

Importance of inpatient hyperglycaemia

Introduction

The management of diabetes over the last 60 years has changed from focussing on the management and prevention of coma, to the prevention of long term micro- and macro-vascular complications. This shift in focus has changed the aim of glycaemic control from sufficient control to keep patients out of hospital, to intensive control aimed at preventing late diabetes complications.¹

Epidemiology of diabetes

Type 2 diabetes is globally the predominant form of diabetes and accounts for 90% of all cases of diabetes. In both developed and developing countries diabetes has become an epidemic and it seems that the burden of this disorder occurs disproportionately in non-European populations: Hispanic, Native American, Pacific and Indian Ocean island populations, with Indian and Australian Aboriginal communities on top of the list. Certain populations where diabetes was practically non-existent 50 years ago now have diabetic populations that constitute 40% of the population, e.g. the Pacific island of Nauru.²

The 2010 global burden of diabetes is estimated to be 285 million people or a prevalence of 6.6% for the age groups 20 to 79 years. This number is expected to rise by 50% over the next 20 years, to 438 million people by 2030 (prevalence of 7.8%).^{2 3}

In South Africa the prevalence of diabetes varies from 3% to 28% depending on the population studied, the age range and whether the population is rural or urban (table 1). With the International Diabetes Foundation estimating the prevalence of diabetes in South Africa in the adult population to be between 4.5% and 5%.³

Table I: Prevalence of type 2 diabetes in different populations in South Africa.⁴

Population	Region (number of participants)	Prevalence (%)	Age range (years)	Reference
African	Cape Town, urban (729)	8.0	30 +	Diabetes Care 1993;16:601
African	QwaQwa, rural (853)	4.8	25 +	S Afr Med J 1995;85:90
African	Mangaung, urban (758)	6.0	25 +	S Afr Med J 1995;85:90
African	Durban, urban (479)	5.3	15 +	S Afr Med J 1993;83:641
Coloured	Cape Town, urban (200)	28.7	65 +	S Afr Med J 1997;87 (suppl 3):364
Coloured	Cape Town, peri-urban (974)	10.8	15 - 86	Diabet Med 1999;16:946
European	Durban, urban (396)	3.0	15 - 69	S Afr Med J 1994;84:257
Indian	Durban, urban (2479)	13.0	15 +	Diabetes Care 1994;17:70

Diabetes in hospitalized patients

Hospitalized patients frequently have diabetes as a co-morbid condition. Because of the nature of diabetes and its related complications, diabetic patients, are more prone to be admitted to hospital. For the non-internist diabetes is frequently a problem that complicates the care of the primary problem for which the patient is admitted.

Three groups of patients can be recognized with inpatient hyperglycaemia. Firstly, patients with known diabetes, admitted for diabetes related or unrelated reasons. Secondly, the group of patients with hyperglycaemia discovered for the first time while in hospital that persists after discharge, and thus constitutes newly diagnosed diabetic patients. The third group of patients are patients who have hyperglycaemia whilst in hospital, which resolves before or after discharge. This third group of patients are often referred to as “hospital related” or “stress” or “transient” hyperglycaemia. The inpatient risk related to the second and third groups of patients seems to be increased (see below). However, up to now no prospective study specifically investigated transient stress related hyperglycaemia as an entity separate from patients with hyperglycaemia in general.⁵

Frequency of admission of diabetic patients

Diabetic patients are more prone to be admitted to hospital and it is a frequent co-morbid condition in hospitalized patients. The relative risk for hospital

admission for people with diabetes is 2.97 and for people with diabetes and hypertension are 3.44 in comparison with patients without these risk factors.^{6,7} In the United States of America diabetes is the fourth most common co-morbid condition complicating all hospital discharges. For example: diabetes was present in 9.5% of all hospital discharges and 29% of all patients undergoing cardiac surgery in 1997.⁶

Diabetes also contributed significantly to prolonged hospital stay, as well as inpatient mortality. The median length of hospital stay was 22 days (2 to 300 days), which is significantly longer than the median stay for all patients in the district (less than 10 days).⁸

Masson et.al.⁸ assessed the outcome of a cohort of diabetic inpatients in an urban health district in the United Kingdom. They found that 8.4% of all hospitalized patients were suffering from diabetes; of these 55% were medical, 16% general surgery patients and the remaining 29% from all other departments. Of all the diabetic patients, 14.5% died during that admission and 10.1% died of macro-vascular disease.

In the study by Robins and Webb⁹ diabetes contributed 32.8% excess odds of rehospitalisation in comparison to patients who did not have diabetes. In 2006 data from the California state inpatient dataset 26.3% of diabetic patients admitted was readmitted within three months of the index admission.¹⁰

Reasons for admission of diabetic patients

Patients with diabetes frequently need admission to hospital for a variety of reasons, which can be related to diabetes or not:¹¹

- Life threatening acute metabolic complications
- Newly diagnosed type 1 diabetes
- Substantial and chronic poor metabolic control that necessitates close monitoring
- Severe chronic complications of diabetes
- Uncontrolled or newly discovered diabetes in pregnancy requiring insulin

- Introduction of insulin pump therapy or other intensive insulin regimens

Jiang ¹² stated that 6.1% of all admissions were for acute diabetic complications, 25.1% had chronic diabetes complications and 91.7% had major cardiovascular diseases including hypertension, in 76.6% of patients.

Diabetic patients are liable to suffer from all other conditions similar to the non-diabetic population and are frequently admitted to hospital for reasons not related to diabetes. In the study by Hongsoo et al.¹⁰ 56.7% of all patients with unscheduled admissions and 57.1% of scheduled admissions were for diabetes complications or for conditions other than the diabetes itself.

Cost of management of diabetic inpatients

Diabetic patients' hospital admissions are costly, and this cost is usually related to complications of the disease.

Jiang et.al.⁷ used the healthcare cost and utilization project data of 1999 of five states of the USA to assess the extent of hospitalizations and costs in patients with diabetes. She concluded that 70% of patients with diabetes were admitted once, 18.1% twice and 11.9% thrice. The average cost of hospital stay was \$ 8 508 for patients admitted once, and \$ 23 119 for patients admitted repeatedly. The average length of stay was 6.8 days for patients admitted once and 7.4 days per stay for those admitted more than once.

Health care cost of people with diabetes is at least 2.5 times more expensive than that of the non-diabetic control populations (matched for age and gender), and about 5 times as expensive as the average for the entire population.⁷

From the Helsinki study¹³ excess cost caused by diabetes inpatients was \$ 25 506 000. This amounts to 55.6% of the total cost of management of inpatients with diabetes. Hospital care contributed 49.5% to the total cost of diabetes care.

The percentage excess cost for hospital care of macro-vascular complications was 17.9%, micro-vascular complications was 4.9% and for illness unrelated to diabetes 28.7%.

From a recently published study assessing the cost of hospital care for patients with diabetes; the mean cost per admission for patients with diabetes is £ 2 103.90 in comparison to that for non-diabetic patients of £ 1 487.00.¹⁴

Glycaemic control and outcome

Strong evidence of improved hospital outcomes exist for patients in intensive care and coronary care settings using intravenous infusions of insulin, but data for general medical and surgical inpatients similar outcome data is sparse. There is a lack of randomized clinical trials in settings outside intensive care and coronary care units.¹⁵

Physiological mechanisms explaining hyperglycaemia in patients, experiencing stress due to disease, which require hospital admission, are well described. These conditions promote a decrease in insulin secretion and induce an increase in insulin resistance. Protection against adverse outcomes may be influenced by numerous metabolic and non-metabolic mechanisms related to control of hyperglycaemia.¹⁵

Sufficient evidence is available to confirm that blood glucose control is extremely important in the management of diabetes, whether as an in- or out-patient. Complications are seen more often in diabetic patients who are seriously ill, have wounds or are undergoing surgery. This applies to patients who are known to have diabetes as well as undiagnosed patients presenting with hyperglycaemia for the first time on admission.

Inpatients admitted to general hospital wards

Umpierrez et.al.¹⁶ reviewed 1886 admissions for the presence of hyperglycaemia (fasting glucose ≥ 7 mmol/l or random ≥ 11.1 mmol/l on two or more occasions) in surgery and general medicine patients in a community teaching hospital. Of the patients admitted to hospital 26% were known to have diabetes and an additional 12% previously undiagnosed with diabetes had hyperglycaemia first detected in hospital.

After adjusting for confounders the group with newly diagnosed hyperglycaemia had an 18-fold increase in in-hospital mortality. Patients with

known diabetes had a 2.7-fold increase in comparison with normoglycaemic patients. The length of hospital stay was higher for the new hyperglycaemia and known diabetic patients (9 ± 0.7 , 4.5 ± 0.1 and 5.5 ± 0.2 days). New hyperglycaemic and diabetic patients were more likely to need ICU care in comparison to normoglycaemic patients (29% vs. 14% vs. 9%, $p < 0.01$). From this study it can be concluded that in both medical and surgical patients an elevated blood glucose contribute significantly to the length of hospital stay, mortality and morbidity.

In a recently published meta-analysis of studies on glycaemic control in non-critically ill hospitalized patients, intensive glycaemic control was not associated with an increased risk of death, myocardial infarction or stroke. However, a non-significantly increased risk of hypoglycaemia (RR: 1.58, CI: 0.97 to 2.57) was demonstrated. In surgical settings a decrease in the risk of infection was detected (RR: 0.41 CI: 0.21 to 0.77).¹⁷

Davidson et.al.¹⁸ states that two methods are currently used to manage inpatients with diabetes in general wards namely sliding scales and mixed/split insulin regimens.

It is generally accepted that the sliding scale is not very effective, though it is frequently used for its simplicity. The major drawback of the sliding scale is that the physicians wait for the blood glucose to elevate to a certain level before action is taken. Although never proven with a randomized controlled trial, it is assumed that the mixed/split regimen with addition of supplemental or correction dosages of short acting insulin is superior to a sliding scale. This regimen is an attempt to prevent hyperglycaemia before it occurs. Davidson et al.¹⁸ compared two six-month periods; in the first six months patients were treated with sliding scale regimens and in the second six months with a mixed/split regimen with supplemental insulin related to meals. The outcome was as follows: there was a trend towards fewer days in hospital with the mixed/split regimen period although it was non-significant ($p = 0.556$). No significant difference could be demonstrated in glucose control between the two treatment regimens ($p = 0.534$). This inability of the study to show superiority of the mixed/split regimen was ascribed to the short period of patient hospital stay.

In a study by McAlister et.al.¹⁹ hyperglycaemia on admission was independently associated with adverse outcomes in patients with community acquired pneumonia. A cohort of 2471 patients with community acquired pneumonia was observed for hyperglycaemia. Patients with an admission glucose of > 11 mmol/l showed an increased mortality compared to patients with blood glucose \leq 11 mmol/l (13% vs. 9%, $p = 0.03$). For each 1 mmol/l blood glucose increase the risk of in-hospital complications increased by 3% (0.2 - 6%).

Critically ill patients admitted to Intensive Care Units

Van den Berghe et.al.²⁰ did a prospective randomized controlled study of 1548 adult patients who were admitted to a surgical ICU and were receiving mechanical ventilation. The spectrum of patients included cardiac surgery, cerebral trauma or brain surgery, other thoracic surgery, abdominal surgery, vascular surgery, extensive trauma, burns and transplant surgery patients. All included patients had hyperglycaemia irrespective of whether it was stress related, newly diagnosed diabetes or known diabetic patients. Patients were randomized to receive intensive insulin therapy where blood glucose was maintained between 4.4 and 6.1 mmol/l or conventional therapy with target blood glucose of 10 to 11.1 mmol/l.

Intensive insulin therapy reduced the mortality during ICU care from 8.0% in the conventionally treated patient group to 4.6% ($p < 0.04$). This study indicated that the risk of death in ICU increased by 30% for every 1.1 mmol/l the blood glucose was above 5.5 mmol/l. The highest survival rates were achieved in patients where the average blood glucose was below 6.1 mmol/l. However, since the van Berghe study other prospective randomised controlled trials attempting to obtain optimal glycaemic control shows conflicting results for critically ill patients. In a meta-analysis (which included the NICE SUGAR study) where all ICU patients (medical and surgical) are included the Relative risk (RR) for mortality between patients on intensive insulin treatment and conventional insulin treatment is 0.93 (CI 0.83 to 1.04). For purely medical ICUs the RR is 1 (CI 0.78 to 1.28), for mixed medical and surgical ICUs the RR for mortality is 0.99 (CI 0.87 to 1.12). However, for

purely surgical ICU the RR for mortality is 0.63 (CI 0.44 to 0.91). In this group one study contributed overwhelmingly to this beneficial effect (van den Berghe), and all the other studies were small and not significant.²¹

Patients with Myocardial Infarctions

In the DIGAMI ²² study 620 patients with an acute myocardial infarction and hyperglycaemia were randomized to receive intensive therapy, which consisted of insulin infusions, and followed by a 3 month multiple injection regimen. This group achieved mean blood glucose of 9.6 mmol/l. The conventional treatment arm had a mean blood glucose of 11.7 mmol/l. Mortality at one year in the intensive treated group was 18.6% and in the conventionally treated group 26.1% (p = 0.027). This benefit extended to at least 3.4 years.

The DIGAMI 2 ²³ study was designed to answer the question if in addition to the strict peri-infarction period, a longer term glycaemic control would improve the outcome further. The DIGAMI 2 study randomized 1253 type 2 diabetic patients post myocardial infarction to one of three groups of care after the initial intensive insulin based glycaemic management in hospital. The three groups were: Insulin based long-term glucose control, standard glucose control and routine metabolic management according to local practice. At baseline the group characteristics were the same. The median study duration was 2.1 years (Interquartile range: 1.03 to 3.00 years). The results: 42% of patients in the insulin based long term glucose control group received multidose insulin daily compared to 15% and 13% of patients in the other two groups respectively. At the end of follow up the HbA1c did not differ significantly between the 3 groups. The mortality between the groups also did not differ significantly; 23.4%, 22.6% and 19.3% respectively for the three groups. The target blood glucose of 5 to 7 mmol/l for the insulin based treatment group was never achieved.

Patients peri-surgery

In a study by Furnay et.al.²⁴ it was demonstrated that a continuous insulin infusion reduced the mortality of patients with diabetes undergoing coronary bypass surgery

Pomposelli et.al.²⁵ studied 97 patients undergoing general surgery. Blood glucose was monitored every 6 hours. It was found that a single blood glucose measurement >12.2 mmol/l on the first post-operative day was a sensitive (85%) but relatively nonspecific (35%) predictor of nosocomial infections. Patients with a blood glucose of >12.2 mmol/l had infection rates 2.7 times higher than those with blood glucose lower than 12.2 mmol/l. When minor infections were excluded the relative risk (RR) for serious infections post operatively was 5.7.

Zerr et.al.²⁶ conducted a study in cardiac surgery patients from 1991 to 2001 with management of blood glucose to a target: 8.3 to 11.1 mmol/l. An optimal blood glucose in the first 2 days post surgery resulted in a reduction of deep wound infections from 2.4% down to 1.5% ($p \leq 0.02$). Within the same study in Portland the risk of death was decreased by 60% (RR = 0.04), this was due to a reduction in heart failure and arrhythmias.²⁷

Diabetic patient management in hospital

Management of inpatients suffering from diabetes should be matched to the patient's specific circumstances and disease severity. Patients with hyperglycaemia can be categorized according to the inpatient situation, which will determine what type of treatment regimen should be followed (table II). At present guidelines do not differentiate between the management of hyperglycaemia in diabetic patients and patients with transient stress induced hyperglycaemia. The glycaemic targets for both these groups are the same and the means to achieve these do not differ.²⁸

Diabetes is frequently not diagnosed before admission. Even after admission an alarming proportion of patients will not have been recognized as having hyperglycaemia. Levetan et.al.²⁹ report a prevalence of laboratory documented hyperglycaemia in 13% of hospitalized patients; of these 64%

had pre-existing hyperglycaemia or new onset diabetes. Thirty six percent of these remained unrecognized as having diabetes in an audit of discharge summaries.

All doctors caring for patients irrespective of the discipline in which they work should be familiar with the management of diabetes, and need to be able to fit the correct treatment protocol to his/her patients. All nursing staff irrespective of the nursing unit where they work should know how patients with diabetes should be managed.^{30 31}

The AACE and ADA³² recommend the following:

In critically ill patients:

- Insulin therapy should be started for persistent hyperglycaemia, starting at a threshold of 10 mmol/L.
- Glycaemic target should be 7.8 to 10 mmol/L.
- Intravenous insulin infusion is preferred and should preferably be administered using a validated protocol with a low rate of hypoglycaemia.
- Frequent blood glucose monitoring is essential.

Non critically ill patients:

- Pre-meal glycaemic target should be less than 7.8 mmol/L and random blood glucose values should be less than 10 mmol/L, provided that it can be achieved safely.
- More strict control may be appropriate in stable patients with previously tight control.
- Less strict targets may be appropriate in patients with terminal illness or severe co-morbidities.
- Scheduled subcutaneous insulin should be administered to supply basal and prandial requirements as well as supplemental (adjustment or correcting) dosages of insulin.
- The use of sliding scales only is strongly discouraged.

Additional issues in inpatient diabetes management

Inpatient glucose monitoring

Blood glucose monitoring for inpatients with diabetes is analogous to an additional vital sign. This can be achieved today by rapid capillary blood glucose determinations; these blood glucose determinations can and should be performed by adequately trained personnel. The use of bedside glucose monitoring requires:³³

- a clear administrative responsibility for the procedure
- a well defined policy and procedure manual
- a training program for personnel doing the testing
- quality control procedures
- regular and scheduled equipment maintenance.

The American Diabetes Association advises bedside glucose monitoring using capillary blood due to the rapidity of the result, which allows for point of care decisions on therapy. For patients that are eating, it is recommended to test before meals and at bedtime. For non-eating patients testing at 4 to 6 hour intervals is recommended. For patients controlled with intra-venous insulin, it is advised that testing be done hourly until the blood glucose is stable, thereafter every 2 hours. ³⁴

Table II: Guideline for in-hospital management of diabetes and hyperglycaemia. ^{5 21 35 36}

Clinical setting	Comments	Scheduled insulin		Supplemental / correctional
		Basal	Prandial / nutritional	
Eating patients well controlled on home regimen	Type 2 patients only on oral agents should continue with home treatment unless contraindicated (if contraindicated manage same as type 1 patients)			Regular or Rapid acting insulin before meals according to scale
	Type 1 diabetic patients should continue with home insulin schedule but consider reducing the total daily dose if caloric intake will be more restrictive			Regular or Rapid acting insulin before meals according to scale
Eating patients poorly controlled on home regimen	Type 2 patients should continue with insulin sensitizers unless contraindicated	0.2 to 0.3 U/kg/day NPH insulin or Detemir 12 hly or Glargine daily. Adjust daily to pre-breakfast glucose value	Regular or Rapid acting insulin. Start with 0.05 to 0.1 U/kg/meal or 1 U/15g carbohydrate. Adjust daily according the need for supplemental insulin	Regular or Rapid acting insulin before meals according to scale
Peri-operative or peri-procedural but will eat afterwards	If in doubt start patient with insulin infusion	Give usual basal insulin	Commence with prandial insulin as above as soon as patient starts to eat	Regular insulin 4 to 6 hly or Rapid acting insulin 4 hly according to scale
Peri-operative or peri-procedural but will not eat afterwards	Insulin infusion preferable during procedure but can be continued afterwards	Give usual basal insulin	N/A	Regular insulin 4 to 6 hly or Rapid acting insulin 4 hly according to scale
Continuous enteral feeding (TEN)	Consider insulin infusion, adjust infusion rate until control is achieved	Give 40% of daily requirement. NPH insulin or Detemir 12 hly or Glargine daily.	N/A	Regular insulin 4 to 6 hly or Rapid acting insulin 4 hly according to scale
Bolus enteral feeding		Give 40% of daily requirement. NPH insulin or Detemir 12 hly or Glargine daily.	Regular or Rapid acting insulin. Start with 0.05 to 0.1 U/kg/bolus or 1 U/15g carbohydrate.	Regular insulin 4 to 6 hly or Rapid acting insulin 4 hly according to scale during bolus period
Continuous parenteral feeding (TPN)	Insulin infusion, adjust infusion rate until control is achieved			
Critically ill patient	Insulin infusion, adjust infusion rate until control is achieved then maintain			

Patient diabetes education

Patients admitted to hospital for whatever reason opens a unique opportunity to educate patients to improve patient knowledge of diabetes and to improve patient self-management skills.^{36 37}

Roman and Chassin³⁸ conducted a study to assess the knowledge of inpatients with diabetes as well as glycaemic control post discharge. They noted that glycaemic control significantly improved after education. They however also found that 40% of patients still had important diabetes knowledge deficits post discharge.

Nutritional care

A registered dietician is a crucial team member in the in- and outpatient management of patients with diabetes. Two important aspects can be addressed specifically while patients are admitted to hospital: nutritional assessment and nutritional intervention. Once again the opportunity of educating patients with diabetes on nutritional issues during admission is an optimal situation in which the patient can be exposed to nutritional caregivers repeatedly.^{39 40}

Discharge planning

All diabetic patients should have a post discharge plan. This includes follow up with an appropriate caregiver who is capable of taking care of diabetes and diabetes related problems. It should also be confirmed that the patient and preferably their families should be familiar with outpatient glucose targets. Attempts should be made to introduce the home diabetes management regimen to the patient whilst still in hospital.^{15 36}

Workup opportunity and risk factor assessment

Hospitalization creates the perfect opportunity for the evaluation of patients with diabetes with specific reference to assessment of micro- and macro-vascular complications namely nephropathy, retinopathy, neuropathies, and

cardiovascular disease. The assessment of risk factors and the control thereof is ideal since fasting bloods can easily be taken, and a profile of blood pressure over a 24-hour period can be obtained. This opportunity should be structured to obtain the most information related to the prevention and care of complications in these patients during admission.³⁶

Education of caregivers

Bernard et.al.⁴¹ stated that a significant barrier to improvement of diabetes care, is that most trainee physicians do not think additional training in diabetes care is necessary. Resident physicians felt that a lack of time is a greater barrier to the quality of patient care than a deficiency of training. It was hypothesized that the difficulty with residents' diabetes practices could be the result of a lack of knowledge and experience of supervising physicians.

Baldwin et.al.⁴² demonstrated that a systematic approach to education of residents in inpatient diabetes management could improve the care of hospitalized diabetic patients.

A number of studies assessing nurses' knowledge and behaviour after an education program concluded that a discrepancy exists between the knowledge and behaviour of nurses caring for diabetic patients. It seems that nurses primarily change their clinical practice from new knowledge obtained from unit-based resources. It is recommended that nurse training should focus on unit-based training.^{43 44}

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