MYANMAR GUIDELINE ON

GLYCEMIC MANAGEMENT OF TYPE 2 DIABETES MELLITUS

2024

Foreword

President of MMDA

I am honored to introduce the Myanmar Diabetes Guidelines, a comprehensive resource that reflects the collective dedication of healthcare professionals and experts in our pursuit of combating diabetes in Myanmar. As diabetes continues to pose a significant health challenge, these guidelines serve as a beacon of knowledge and guidance.

In navigating the intricacies of diabetes management, these guidelines provide a roadmap for healthcare practitioners, empowering them to deliver informed and effective care. The collaborative efforts behind this initiative underscore the commitment to improving the health and well-being of our communities.

As we delve into these guidelines, let us recognize the importance of awareness, education, and early intervention in the fight against diabetes. Together, we can make a meaningful impact on the lives of those affected and strive towards a healthier future for Myanmar.

I extend my deepest appreciation to all those involved in bringing these guidelines to fruition. May this resource contribute significantly to the advancement of diabetes care in our nation.

Professor Tint Swe Latt
President
Myanmar Diabetes Association

Foreword

Vice President of MMDA

The rising incidence of diabetes mellitus is an issue of global concern. The prevalence of type 2 diabetes mellitus among adults is 10.8% in Myanmar and it is also in a rising trend. Apart from a negative impact on the quality of life and health care costs, diabetes also increases the economic burden of individuals, families and communities and affects national productivity.

As the type 2 diabetes is a chronic complex disease the management requires multifactorial approaches with individualized treatment regimens.

The therapeutic targets should be aiming to reduce the complications, maintain the quality of life and prevention of early death. This includes management of hyperglycemic, over-weight, cardiovascular risk factors, comorbidities and complications.

Although we already had published guidelines for Diabetes management and guideline for insulin therapy before it is necessary to update our health care providers including primary care physicians with this new guideline because of the following reasons. Several Cardiovascular Outcome trials (CVOTs) from 2 new classes of glucose-lowering agents have shown cardio-vascular (CV) protection, beyond glucose. The findings from these landmark trials have changed clinical pathways and recommendations in the way T2DM is managed. Nevertheless, we have to follow individualized approach as majority of our patients may not be accessible to these new drugs.

The workgroup has carried out a thorough review of literature to formulate these guidelines. So, this guideline would provide the HCP with the latest best practice information regarding the clinical management of hyperglycemia in T2DM, based on the best available evidence at the time of development.

I would like to congratulate all the task force members for their immense support and contribution, and I am sure these updated guidelines will assist clinicians in improving the standard of diabetes care and reduce the burden of T2DM in our country.

Last but not least I would like to express my gratitude to everyone involved in the development of this guideline for Glycemic management of type 2 diabetes mellitus in Myanmar.

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Myanmar Guideline on Glycaemic Management of Type 2 Diabetes Mellitus 2024

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GLYCEMIC MANAGEMENT OF TYPE 2 DIABETES MELLITUS

2024

Glycemic Management of Outpatients

Treatment Algorithm

Lifestyle Modification to all Patients

Glycemic Management

HbA1c < 8.5% OR FPG < 150 mg/dL, < 8 mmol/L RBS < 250 mg/dl, < 13 mmol/L	HbA1c 8.5% - 10.0% OR FPG 150 - 250 mg/dL, 8 - 13 mmol/L RBS 250 - 350 mg/dl, 13 - 19 mmol/L	HbA1c > 10% OR FPG > 250 mg/dL, > 13 mmol/L RBS > 350 mg/dl, > 19 mmol/L
Monotherapy	Dual combination therapy*	Triple combination therapy** (or Insulin if osmotic symptoms or weight loss present) ++
Metformin *	Metformin *	Metformin *
Sulfonylurea	Sulfonylurea	Sulfonylurea
DPP4-i	DPP4-i	DPP4-i
SGLT2-i	SGLT2-i	SGLT2-i
Insulin	AGI	AGI
▪ Follow up with Blood Glucose level after **2-4 weeks.** ▪ Optimize dose of OAD / addition of another OAD in subsequent **2-4 weeks.** ▪ HbA1c every **3-6 months**	TZD	TZD
• If blood glucose level is satisfactory and / or HbA1c reach individualized target, continue therapy ***	Insulin	Insulin
	GLP1-RA	GLP1-RA
	▪ Follow up with Blood Glucose level after **2-4 weeks.** ▪ Optimize dose of OAD / addition of another OAD in subsequent **2-4 weeks.** ▪ HbA1c every **3-6 months**	▪ Follow up with Blood Glucose level after **2-4 weeks.** ▪ Optimize dose of OAD / addition of another OAD in subsequent **2-4 weeks.** ▪ HbA1c every **3-6 months**
	• If blood glucose level is satisfactory and / or HbA1c reach individualized target, continue therapy ***	• If blood glucose level is satisfactory and / or HbA1c reach individualized target, continue therapy ***

Efficacious, low risk of hypoglycemia and weight neutral

Efficacious, risk of hypoglycemia and weight gain

Efficacious, low risk of hypoglycemia and weight loss

Moderate efficacy, low risk of hypoglycemia and weight neutral

Moderate efficacy, low risk of hypoglycemia and weight gain

Moderate efficacy, low risk of hypoglycemia and weight loss

Modest efficacy, low risk of hypoglycemia and weight neutral

* Metformin should be first line unless contraindicated

** Start with low dose: Optimize dose of OAD / addition of another OAD in subsequent 2-4 weeks.

*** If blood glucose level and HbA1c is discordant, look for the reasons of discordance or seek advice from Endocrinologists

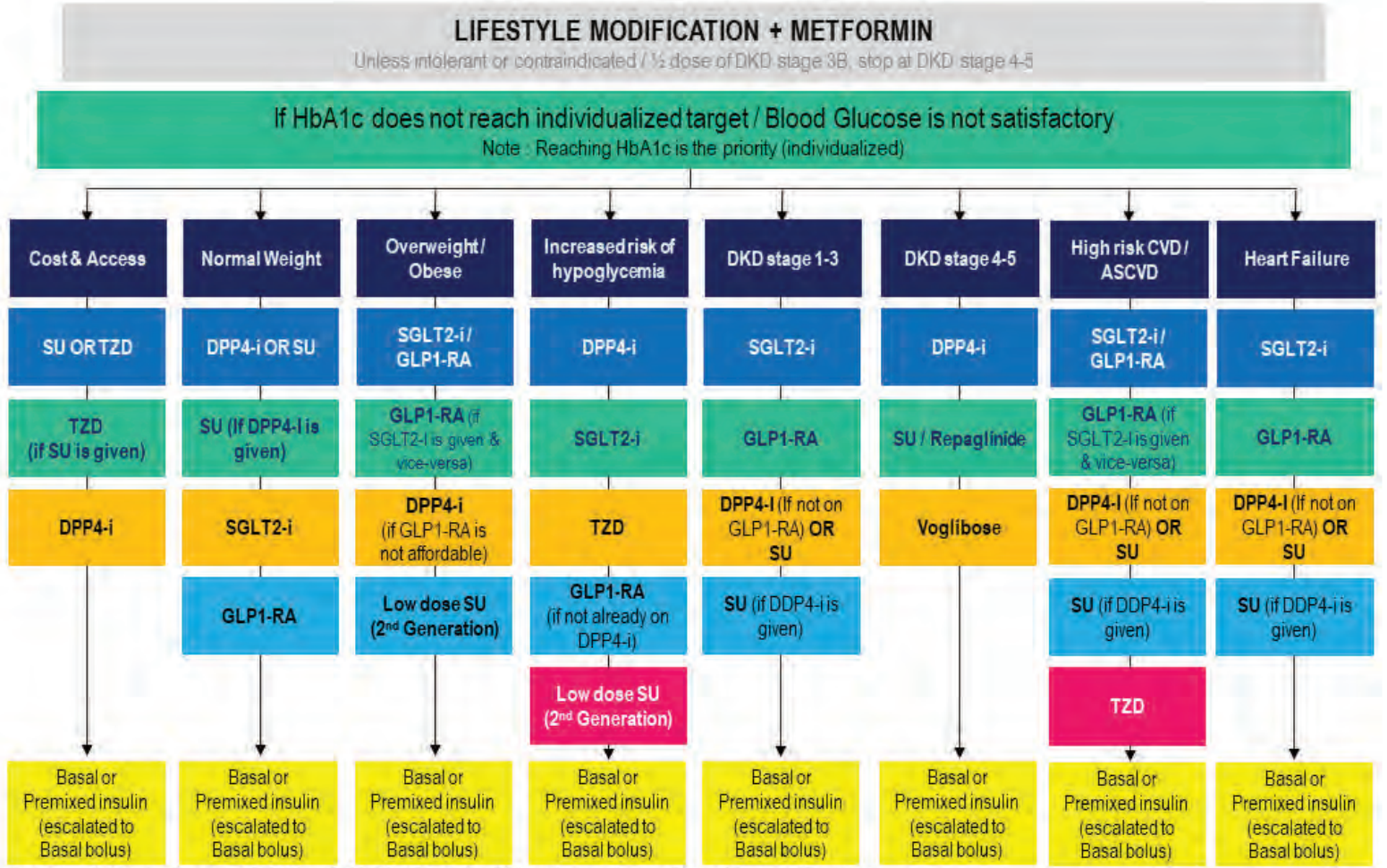
++ Rescue therapy : For symptomatic hyperglycemia, consider insulin or sulfonylurea and review when blood glucose has been

Glycemic Target

HbA1c	<7%*
Preprandial Glucose	80-130 mg/dl*
Postprandial Glucose	< 180 mg/dl*

*More or less stringent individualized glycemic target should be based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individualized considerations

Individualized Choice of Anti-diabetic Drugs



1.in terms of choosing between SGLT2i or GLP1-RA, SGLT2i should be prioritized according to Myanmar Situation
2.DKD 1-3 : e GFR ≥ 30 ml/min, DKD Stage 4-5 : eGFR < 30ml/min 3.Sulfonylurea and Repaglinide should not be used together because of similar site of action

Dosage of Oral Anti-diabetic drugs in renal failure

Generic Name	Usual dose	Dose adjustment in renal failure		
		Mild (CKD 2) (GFR 60-89)	Moderate (CKD 3) (GFR 30-59)	Severe (CKD 4 & 5) (GFR <30)
Biguanide				
Metformin	500 -1000 mg BD	Continue	45-60: No dose adjustment	Avoid
Metformin SR	500 -1000 mg BD 750 mg BD 850 mg BD		<45: 50% dose reduction	
Sulphonylurea				
Gliclazide	80 mg OD-160 mg BD	No dose adjustment		Caution
Gliclazide MR	30-120 mg OD	No dose adjustment		Caution
Glimepiride	1-6 mg OD	Initiate with 1 mg OD		≥15: Caution
Glipizide	2.5 mg OD-10 mg BD	No dose adjustment		Caution
Meglitinides				
Repaglinide	0.5-4 mg TDS	No dose adjustment		Initiate at 0.5 mg with meals
Alpha-glucosidase Inhibitor				
Acarbose	25-100 mg TDS	50-100%		≥25: 50-100%
Voglibose	0.2-0.3 mg TDS	No dose adjustment		
Thiazolidinediones				
Pioglitazone	15-45 mg OD	No dose adjustment **(caution with fluid retention risk)**		
DPP4-i				
Sitagliptin	100 mg OD	No dose adjustment	≥50: No dose adjustment	25 mg OD
			30-<50: 50 mg OD	
Vildagliptin	50 mg OD-BD	No dose adjustment	≥50: No dose adjustment	
			<50: 50 mg OD (limited data)	
Teneligliptin	20-40 mg OD	No dose adjustment		
Linagliptin	2.5-5 mg OD	No dose adjustment		
GLP1-RAs				
Liraglutide	1.2 to 1.8 mg OD (initial 0.6 mg OD x one week)	No dose adjustment	No dose adjustment	≥15: No dose adjustment / <15: Avoid
SGLT2 Inhibitors				
Dapagliflozin*	5-10 mg OD	No dose adjustment	45-60: No dose adjustment	Avoid
			<45: Not recommended	
Canagliflozin	100-300 mg OD	No dose adjustment	100 mg OD	Avoid
Empagliflozin	10-25 mg OD	No dose adjustment	No dose adjustment	Avoid
Insulin				
Doses should be adjusted based on frequent monitoring to balance goals of glycaemic control with avoiding hypoglycaemia. Long-acting tends to accumulate longer than short-acting insulin.				

**Dapagliflozin can be given up to eGFR 25 ml/min for Heart Failure and Chronic Kidney Disease.*

Efficacy of Various Anti-Diabetic Drugs

	MET	SU	GLN	AGI	TZD	DPP4-i	SGLT2-i	GLP1-RA	Insulin
HbA_{1c} ↓ %	1.0-1.5	0.4-1.6	1.0-1.2	0.5-0.8	0.5-1.4	0.5-0.8	0.2-0.8	0.5-1.4	>1.5
FPG vs. PPG	FPG	Both	PPG	PPG	FPG	Both	Both	Both	Both
Hypoglycaemia	↔	↑↑	↑	↔	↔	↔	↔	↔	↑↑
Weight change	↓	↑↑	↑	↔	↑↑	↔	↓–↓↓	↓↓	↑↑
GI symptoms	↑↑	↔	↔	↑↑	↔	↑	↔	↑↑	↔
CHF	↔	↔	↔	↔	↑	↔	↓↓	↔	↔
CVD	↓	↔	↔	↔	↔	↔	↓↓	↓↓	↔
Bone loss	↔	↔	↔	↔	↑	↔	↔	↔	↔
DKD	Avoid*	Hypo	Hypo	↔	Fluid ret'n	Dose adjustment	↓↓[a]	↓[†]	Hypo

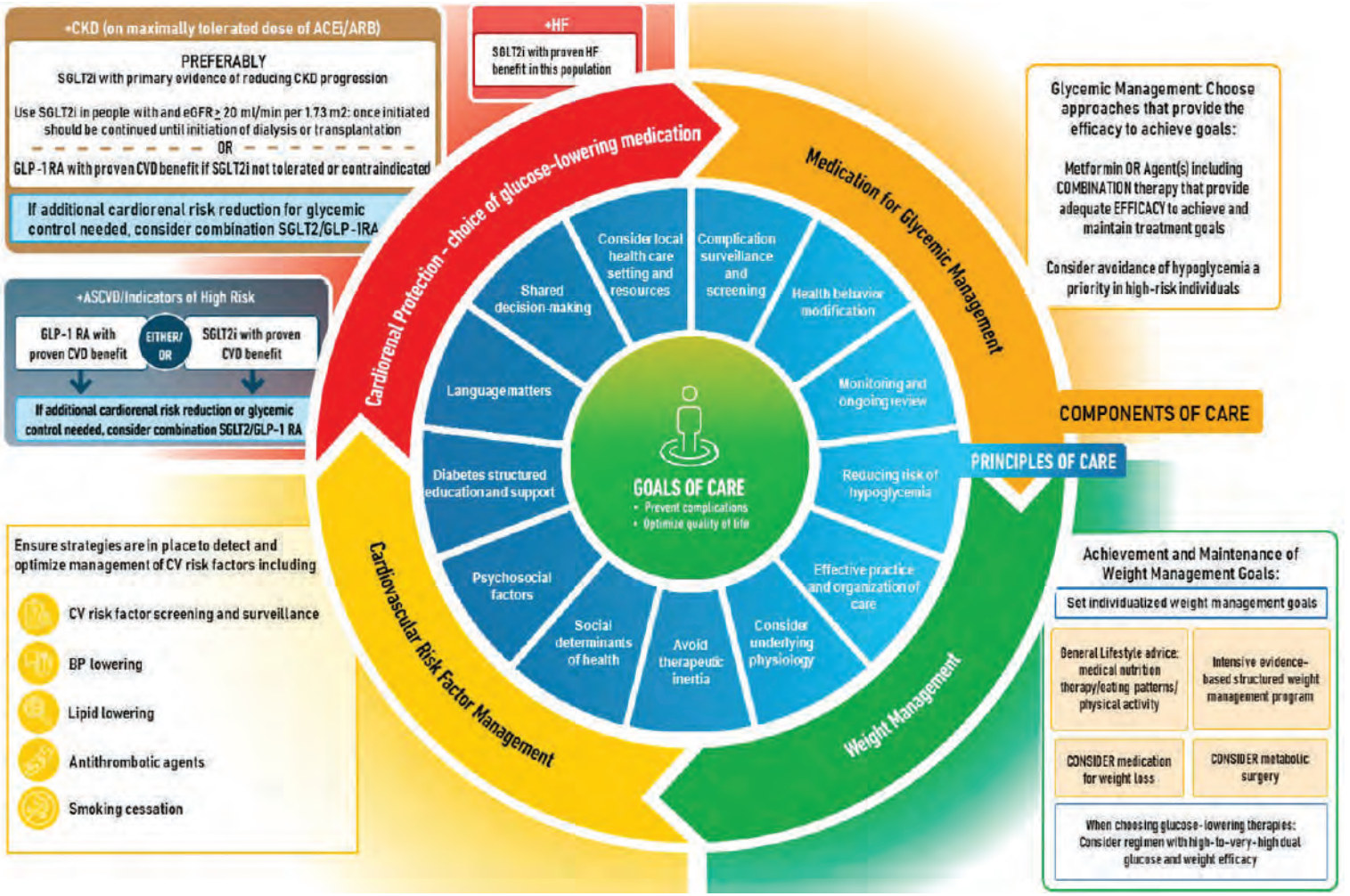
** Avoid if eGFR < 30ml/min/1.73m²; [†]avoid if eGFR < 15 ml/min/1.73m²; [a]SGLT2-i can be used until dialysis is initiated and has proven reno-protection although glucose-lowering efficacy is reduced.*

Increased risk *Mild-mod risk* *Neutral* *Possible benefit* *Beneficial*

Oral Anti-diabetic drugs & Injectable Non-insulin Agents

Drugs	Formulation	Minimum dose	Maximum dose
Biguanides			
Metformin	500/1000 mg	Initial dose: 500 mg OD	Usual: 1000 mg BD *Exception: 1000 mg TDS
Metformin SR	500/750/850/.1000 mg	Initial dose: 500 mg OD	850 mg TDS 2000 mg OD
Sulphonylureas			
Gliclazide	80 mg	40 mg OM	160 mg BD
Gliclazide MR	60/30 mg	30 mg OM	120 mg OM
Glipizide	5 mg	2.5 mg OM	10 mg BD
Glimepiride	2/3 mg	1 mg OM	6 mg OM
Meglitinides			
Repaglinide	0.5/1/2 mg	0.5 mg with main meal	4 mg with main meals (not exceeding 16 mg daily)
α-glucosidase inhibitor			
Acarbose	50/100 mg	Initial dose: 50 mg OD Usual dose: 50-100 mg take at 1st bite of main meals	100 mg TDS
Voglibose	0.2/0.3 mg	0.2 mg TDS (with meal)	0.3 mg TDS (with meal)
Thiazolidinedione			
Pioglitazone	15/30 mg	15 mg OD	45 mg OD
DPP4-inhibitors			
Sitagliptin	25/50/100 mg	25 mg OD	100 mg OD
Vildagliptin	50 mg	50 mg OD	50 mg BD
Teneligliptin	20/40 mg	20 mg OD	40 mg OD
Linagliptin	5 mg	5 mg OD	5 mg OD
SGLT2-inhibitors			
Dapagliflozin	5/10 mg	5 mg OD	10 mg OD
Canagliflozin	100/300 mg	100 mg OD	300 mg OD
Empagliflozin	10/25 mg	10 mg OD	25 mg OD
GLP1-RA			
Liraglutide	6 mg/mL	0.6 mg OD	1.8 mg OD

Holistic Person-Centered Approach to T2DM Management



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Inpatient Glycemic Management

Inpatient Glycemic Management

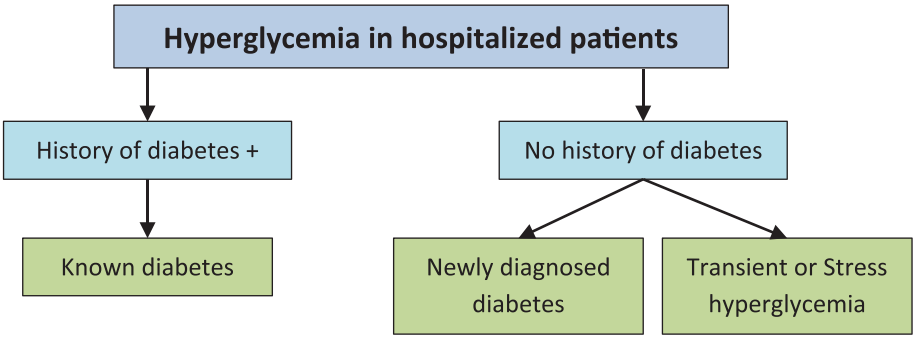
Introduction and definition

- Hyperglycemia in the hospital may result from stress, decompensation of type 1 diabetes, type 2 diabetes, or other forms of diabetes and/or may be iatrogenic due to administration of pharmacologic agents, including glucocorticoids, vasopressors, etc.[2]
- In ADA and AACE consensus on inpatient hyperglycemia, inpatient hyperglycemia is defined as any blood glucose concentration > 140 mg/dl in patients without a prior history of diabetes.[5]
- Approximately, thirty percent of inpatients found to have hyperglycemia which may be due to preexisting diabetes prior to admission or stress hyperglycemia.
- Hyperglycemia influences patient outcomes, including mortality, inpatient complications, length of hospital stay, and overall hospital costs both in critically ill and non-critically ill patients.[1]
- Thus, careful management of inpatient hyperglycemia has direct and immediate benefits.[3]

Screening and monitoring of hyperglycemia

- All patients should check capillary blood glucose (CBG) upon hospital admission independent of prior diagnosis of diabetes.[7]
- Assess all patients for a history of diabetes, prediabetes, type of diabetes and any history of antidiabetic drugs taken. Review most recent HbA1c testing. [8]
- In non-diabetes patients, if CBG > 140 mg/dl , need to monitor CBG for 24-48 hours. In patients with known diabetes, monitor CBG 4 times a day.[7]
- All inpatients with known diabetes or with hyperglycemia > 140 mg/dl be assessed with HbA1c level if this has not been performed in the preceding 2–3 months.[7]

Screening of Hyperglycemia and Diabetes in Hospital Setting [10]



Check BG testing (Capillary - POC +/- Venous) to every patient upon admission

History of DM +	No history of DM
❖ CBG monitoring 4 times a day ❖ Check HbA1C if not done last 3 month	**BG ≤140 mg/dl** → May not need regular BG monitoring unless clinical condition changes** **BG > 140 mg/dl** → ❖ Capillary BG monitoring (6 hourly if not eating or premeal if eating well) ❖ BG monitoring x 24–48 hours ❖ Check HbA1C if Blood Glucose > 140 mg/dl for 2 times over 24 hr
❖ Adjust the dose of usual insulin if already on insulin **OR** ❖ Change to insulin from usual OAD (prefer) **OR** ❖ Can consider OAD (DPP-4 inhibitor) with or without basal insulin in some patients with mild to moderate hyperglycemia	**HbA1C < 6.5** Transient or Stress hyperglycemia **HbA1C ≥ 6 .5** Newly diagnosed DM **Blood glucose > 180 mg/dl x 2 times consecutively** Start insulin

Clinical condition changes**

1. Starting steroids, tacrolimus, octreotide
2. TPN, EN, or other nutrition changes
3. Sepsis

Management of Hyperglycemia in Hospitalized Patients[10]

Critically ill patients	Non critically ill patients	
Variable rate insulin infusion (VRIII)	Orally allowed ❖ Basal bolus insulin (Prefer) OR ❖ Can consider OAD in some minor illness (e.g., AVI, mild infection) with mild to moderate hyperglycemia E.g., DPP4 inhibitor +/- basal insulin	Orally not allowed ❖ VRIII **OR** ❖ Basal Insulin **OR** ❖ Basal +correctional insulin

Target of BG (mg/dl)	
Majority of both critically and non- critically ill patients	140-180 mg/dl
Critically ill post- surgical or cardiac surgical patients	110-140 mg/dl
Patients with severe comorbidities or no close nursing monitoring	180-250 mg/dl
Terminally ill patients with short life expectancy	> 250 mg/dl

Insulin regimens			
Type	**Variable rate insulin infusion (VRIII)**	**Basal bolus insulin+ prandial insulin correction dose**	**Basal insulin or Basal insulin + prandial insulin correction dose**
Indications	❖ Critically ill patients ❖ Who are kept nil by oral ❖ Who are unable to tolerate orally or having persisting vomiting	❖ Suitable for most patients who are not critically ill ❖ Who are able to eat adequate nutrition orally	❖ Who have poor oral intake ❖ Who are kept nil by oral
Monitoring[5]	1-2 hourly	Before meals and before bed-time	4-6 hourly
Single use of sliding scale insulin or GKI is no longer recommended.			
People with type 1 diabetes must be maintained on insulin therapy at all times to prevent DKA.[9]			
Details of insulin prescription refer to “Insulin guideline”			

Discharge Plan[1]

DSME : Every hospitalized patient need DSME

- Healthy eating and lifestyles
- Monitoring of BG
- Targets or goal of BG
- Complications of DM
- How and when to take prescribed diabetes medications
- How to prevent and treat hypoglycemia and hyperglycemia
- Sick day rules and instructions for emergencies
- Follow up plan

Suggested discharge treatment	
HbA1c < 7 %	Restart pre-admission treatment
HbA1c 7 – 9 %	Intensification of pre- admission OAD treatment **AND /OR** Add basal insulin
HbA1c > 9 %	Discharge on basal bolus insulin of same hospital dose **OR** Twice daily premixed insulin **OR** Restart pre- admission oral hypoglycemic agents + addition of basal insulin

Individualized treatment depends on in-hospital insulin requirement may be needed in some patients.

Enteral (EN) and Parenteral (PN) Nutrition

Introduction

- The use of enteral (EN) or parenteral nutrition (PN) is an independent risk factor for new onset or aggravation of inpatient hyperglycemia for patients with or without history of diabetes.
- The prevalence of inpatient hyperglycemia is up to 30% for patients receiving EN and more than 50% for patients receiving PN.[4]

Enteral [12]

Short term - Nasogastric tube feeding
Long term - PEG tube feeding
Methods
1. Continuous (> 24 hr)
2. Cyclical(<24 hr)
3. Intermittent(over 20-60 min every 4-6 hr)
4. Bolus(over 4-10 min)

Parenteral nutrition [11]

Short term-Partial or Peripheral parenteral
Long term-Total or Central parenteral

- Target- critically ill patients(140- 180 mg/dl)
  Non critically ill patient (premeal 100-140 mg/ dL and RBS <180 mg/dL)[4]
- Patients with both type 1 and type 2 diabetes should continue their usual basal insulin at all time in both S/C or IV insulin during EN and PN nutrition.[6]
- Administration of regular insulin at the time of feed commencement is recommended for a bolus feeding regimen.[6]
- Premixed insulin at start and midpoint of feed, or isophane insulin at start and, if necessary, the mid- point of feed are recommended first line options for glycemic management of patients with poorly controlled type 2 diabetes during enteral feeding.[6]

If enteral or parenteral nutrition is initiated[4]

No diabetes
(Start POC BG monitoring 6 hrly)***

Known diabetes
(Continue POC BG monitoring 6 hrly)

BG > 180 mg/dl for 2 times

Insulin therapy

SC insulin

Basal bolus + correction insulin
OR
Basal (NPH bd/tds or Detemir bd or Glargine hs / cm)
OR
Basal + prandial insulin correction

Insulin in TPN bag

At start -regular insulin 1 unit = Carbohydrate 10-15g followed by daily titration of 0.5 unit /10 g of dextrose until target BG.
Correction insulin 4-6 hrly

Separate continuous insulin IV infusion in critically ill or hemodynamically compromised[10] **or marked hyperglycemia**[7]

If feed stopped for > 2 hours, consider IV10% glucose to avoid hypoglycemia

Non-insulin therapy (generally, not consider)

***POC testing can be discontinued** in patients without a prior history of diabetes if BG values are <140 mg/dl without insulin therapy for 24–48 hr after achievement of desired caloric intake.[7]

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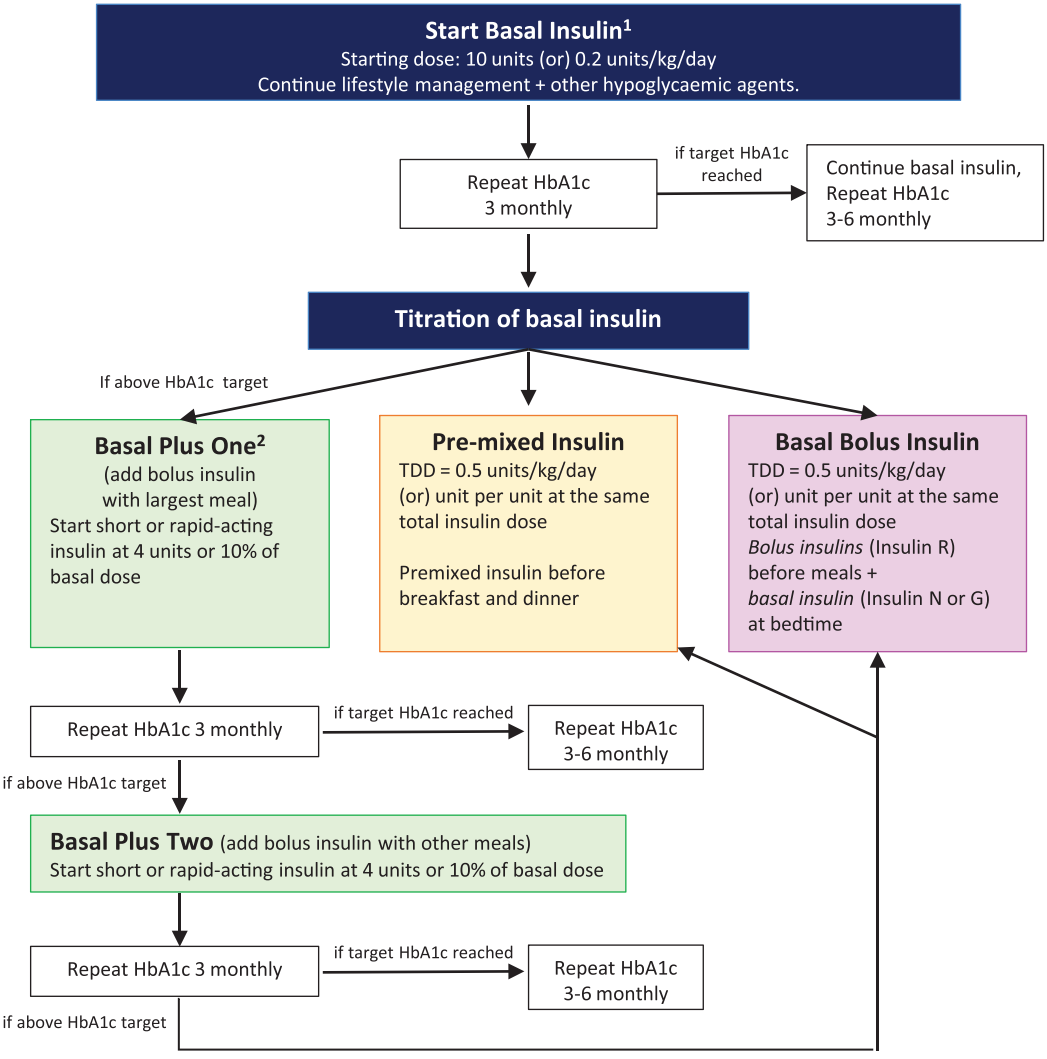
Insulin Therapy

Insulin Therapy

Indications for Insulin therapy in T2DM[1]

- Newly diagnosed patients (with severe osmotic symptoms) if
  - ✓ RBS > 300mg/dl or
  - ✓ FBS >250mg/dl or
  - ✓ HbA1c of ≥ 10%
- Acute clinical conditions (E.g., AMI, Sepsis, Severe Pneumonia, Extensive Koch's Lung etc.)
- Pregnancy (pre-pregnant or GDM)
- Diabetes patients already on OAD therapy (Poor glycaemic control despite maximal tolerable dose of three or four OADs over three months, with HbA1c >7%)



BASAL INSULIN

Intermediate acting (Insulin N): NPH insulin (Insulatard, Insunova N, Wolsulin N, Gensulin N, Maxsulin N)

Long-acting Analogue (Insulin G): Insulin Glargine (Glaritus, Insunova G, Lantus)Detemir (Levemir)

- ❖ Basal insulin is best starting insulin choice.
- ❖ Intermediate and long-acting insulin are comparable in HbA1c lowering effect but less hypoglycaemia with long-acting analogue insulin.
- ❖ Start one of the intermediate-acting or long-acting insulins listed above at bedtime.
- ❖ When starting basal insulin: Continue OAD
- ❖ Note: if NPH causes nocturnal hypoglycaemia, consider switching NPH to long-acting insulin.
- ❖ Let the patient know that food intake is not recommended with basal insulin.
- ❖ Before up-titrating the dose, check the diet first and correct accordingly.

↓

STARTING DOSE:

Start dose: 10 units (or) 0.2 units/kg/day

↓

TITRATE[1]:

Adjust insulin doses after 3 consecutive FBS values obtained (every 3 – 7 days)[3]

- < 80 mg/dL (>1 value) → reduce dose by 2 units
- 80 – 130 mg/dL (all value) → maintain current dose
- >130 mg/dL (>1 value, no hypos) → increase by 2 units

Maximum dose for basal insulin = 0.5/kg/day. If needing more than that, change to other regimen.

↓

Assess adequacy of basal insulin dose[2]

Consider clinical signals of overbasalization (E.g., Basal insulin > 0.5 units/kg/day, elevated bedtime-morning and/or post- pre-prandial differential, hypoglycaemia (aware or unaware), high variability) and need for adjunctive therapies

↓

Once fasting glucose at goal, evaluate post-meal glucose pattern

↓

If post-meal glucose levels > 180: ADD PRANDIAL INSULIN

Note: If patient unable to do multiple daily injections, consider switching to PREMIXED INSULIN BD instead of adding prandial insulin. (Premixed insulin is more likely to cause hypoglycaemia and generally requires a fixed meal schedule)

BASAL PLUS PRANDIAL INSULIN

Basal Plus One = Basal insulin (bedtime) + One Short acting insulin/day (before a main meal)

Basal Plus Two = Basal insulin (bedtime) + Two Short acting insulin/day (before 2 main meals)

Basal Insulin: Insulin N or G

Prandial/Bolus Insulin (Insulin R):

Short Acting (Regular): (Actrapid, Insunova R, Wolsulin R, Gensulin R, Maxsulin R)

Note: Regular insulin has longer peak and extra risk of hypoglycemia.

Rapid Acting (Analogue): Aspart (Novorapid), Glulisine (Apidra), Lispro (Humalog)

- ❖ Add prandial (bolus) insulin to basal insulin if post-meal blood glucose levels are above goal.
- ❖ Start one of the prandial insulins listed above.
- ❖ When adding prandial insulin: Stop secretagogues. Continue metformin. Continue basal insulin (may need to re-adjust dose).
- ❖ Rapid acting insulins should be just before meal. Short acting insulin needs to be taken 30 minute before meals.
- ❖ Before up-titrating the dose, check the diet first and correct accordingly.
- ❖ This regimen is appropriate for patients with fasting and missing a meal. (E.g., Buddhist Monk)

↓

STARTING DOSE:

Start dose for adding one to two bolus: 4 units before each meal (10% of basal insulin) (May consider start with largest meal only.)

↓

TITRATE[1]:

Adjust insulin doses after 3 consecutive days blood glucose values obtained (every 3 – 7 days)[3]

- < 80 mg/dL (>1 value) → reduce dose by 2 units
- 80 – 130 mg/dL (all value) → maintain current dose
- >130 mg/dL (>1 value, no hypos) → increase by 2 units
  - ❖ Pre-lunch blood glucose determines pre-breakfast bolus insulin dose adjustment.
  - ❖ Pre-dinner blood glucose determines pre-lunch bolus insulin dose adjustment.
  - ❖ Bedtime blood glucose determines pre-dinner bolus insulin dose adjustment.
  - ❖ Fasting blood glucose determines bedtime basal insulin dose adjustment.

↓

If target HbA1c not reached after 3-6 months, change to basal bolus or premixed insulin twice daily.

BASAL BOLUS INSULIN

Basal Insulin at bedtime: Insulin N or G

Prandial (Bolus) Insulin before each meal: Insulin R

Short Acting (Regular): (Actrapid, Insunova R, Wolsulin R, Gensulin R, Maxsulin R)

Note: Regular insulin has longer peak and extra risk of hypoglycemia.

Rapid Acting (Analogue): Aspart (Novorapid), Glulisine (Apidra), Lispro (Humalog)

- Basal bolus insulin is an option for patients who[4]
  - ✓ Needs flexibility for work patterns, exercise etc.
  - ✓ Prefers varied diet + timing of meals
  - ✓ Will likely need rapid intensification of insulin therapy
  - ✓ Ability to inject (E.g., cognitive ability, dexterity, supervised environment)
  - ✓ Comfortable with more frequent monitoring and more frequent injections
- Start one of the bolus insulins listed above before meals with basal insulin at bedtime.
- Stop secretagogues. Continue metformin.
- Rapid acting insulins should be just before meal. Short acting insulin needs to be taken 30 minute before meals.
- Before up-titrating the dose, check the diet first and correct accordingly.

↓

STARTING DOSE:

Total Daily dose for basal bolus: 0.5 units/kg/day (or) unit per unit at the same total insulin dose

Conventional: Basal 40%, Bolus 60% (1/3 before each meal)

Analogue: Basal 50%, Bolus 50% (1/3 before each meal)

↓

TITRATE[1]:

Adjust insulin doses after 3 consecutive days blood glucose values obtained (every 3 – 7 days)[3]

- < 80 mg/dL (>1 value) → reduce dose by 2 units
- 80 – 130 mg/dL (all value) → maintain current dose
- >130 mg/dL (>1 value, no hypos) → increase by 2 units

- Pre-lunch blood glucose determines pre-breakfast bolus insulin dose adjustment[5].
- Pre-dinner blood glucose determines pre-lunch bolus insulin dose adjustment[5].
- Bedtime blood glucose determines pre-dinner bolus insulin dose adjustment[5].
- Fasting blood glucose determines bedtime basal insulin dose adjustment[5].

↓

Consider adding pre-meal Correction Factor (CF)[1]
Add 1 unit for each 50 that pre-meal glucose is > 130

Alternative method to determine pre-meal correction factor:
Correction factor (CF) = 1700 / total daily dose of insulin (1700 rule) or 3000/body weight in Kg

PREMIXED INSULIN

Conventional: Combination of short and intermediate acting (30% short + 70% NPH)
(*Mixtard 30, Insunova 30/70, Wolsulin 30/70, Gensulin M30, Maxsulin 30/70, Maxsulin 50/50*)

Analogue: Combination of rapid acting & protaminated analogue (*Novomix 30*),
Combination of Aspart 30% & Degludec 70% (*Ryzodeg*)

- Premixed insulin is an option for patients who are unable to do multiple injections and who have fixed meal schedules.
- Premixed insulin is more likely to cause hypoglycemia compared to basal and prandial insulins.
- Start one of the mixed insulins listed above. Given twice daily, before breakfast and before dinner (or before other meals depending on the main meals, food intake and lifestyle). For analogue insulin, can increase to three times daily before each meal if not well controlled with twice daily regimen.
- Analogue insulins should be just before meal. Conventional insulin needs to be taken 30 minute before meals.
- When starting pre-mixed insulin: Stop secretagogues. Continue metformin. Stop all other insulins.
- Before up-titrating the dose, check the diet first and correct accordingly.

STARTING DOSE:

Total Daily dose: 0.5 units/kg/day (or) unit per unit at the same total insulin dose

Conventional: Morning 2/3, Evening 1/3
Analogue: Morning 50%, Evening 50%

TITRATE[1]:

Adjust insulin doses after 3 consecutive days blood glucose values obtained (every 3 – 7 days)[3]

- < 80 mg/dL (>1 value) → reduce dose by 2 units
- 80 – 130 mg/dL (all value) → maintain current dose
- >130 mg/dL (>1 value, no hypos) → increase by 2 units

- ✓ Pre-lunch and Pre-dinner blood glucose determines morning premixed dose adjustment.
- ✓ Bedtime and Pre-breakfast blood glucose determines evening premixed dose adjustment

ADDITIONAL INFORMATION

Other diabetes medication in combination with insulin[6]

Metformin: Continue if no contraindication because helps prevent weight gain when patient on insulin and reduce insulin resistance.

Secretagogues: (sulfonylureas and meglitinides): Consider continuing when patient is on basal insulin only. Stop when patient is on prandial or mixed insulin.

Other Diabetes Medications: decision to continue or discontinue other diabetes medications should be made with consideration of multiple individual patient characteristics. In individuals with suboptimal blood glucose control, especially those requiring large insulin doses, adjunctive use of a thiazolidinedione or an SGLT2 inhibitor may help to improve control and reduce the amount of insulin needed, though potential side effects should be considered. For individuals with type 2 diabetes with or at high risk for atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease, SGLT2i should be continued.

Note*:* once patient's glucose levels are controlled with insulin, it may occasionally be possible to stop insulin and continue or switch to oral medications depending of the stage of the diabetes and changes in other individual patient characteristics.

Example of correction factor using 1700 Rule[6]
Total Daily Dose (TDD) is 40 units. Correction Factor (CF) = 1700 / 40 = 42. If pre-meal glucose is 250, blood glucose is 120 mg/dl above goal of 130; Correction is 120/42 = 3 units. Give 3 units in addition to prandial insulin dose being used to cover meal.

Mealtime Advice[6]
Take rapid acting prandial and mixed insulins just before a meal. At restaurants only take once food actually arrives at table. Take Regular insulin 30 minutes before meals.

Hypoglycaemia[6]
Tell patient to carry rapidly absorbed carbohydrate source at all times and teach friends and family about how to treat low glucose. Treat low glucose (<70) as per **Rule of 15's**: Give 15 gm of rapidly absorbed carbohydrate (i.e.: 3 teaspoonful of sugar). Recheck glucose level in 15 minutes. Give another 15 gm of carbohydrate if glucose still < 70. Repeat until the glucose level is > 70. Once glucose level returns to normal, consider follow with a snack or meal. Inform provider of hypoglycaemia episodes at next appointment.

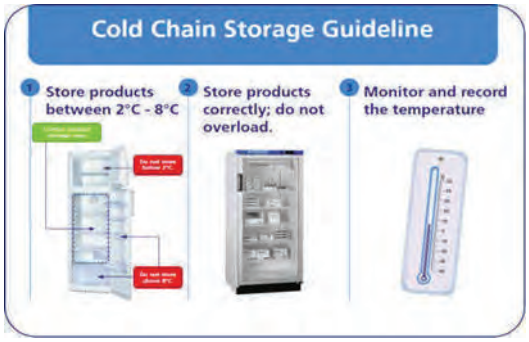
Exercise[6]
Low glucose levels may occur during or after exercise. Carry glucose source when exercising. Check glucose before and during exercise. If patient has low glucose levels associated with exercise: consider decreasing preceding prandial insulin dose (if within several hours before exercise) and/or taking extra carbohydrates before or during exercise.

Insulin Device[6]
Consider insulin pen if able for patients with vision, dexterity or cognition difficulties or for patient convenience. Furthermore, insulin pens are more accurate than syringes for doses of insulin and are less painful. Note insulin pens cost more than insulin vials. However, total cost of insulin pen is potentially lower than vial if patient's daily insulin dose is low (since less unused insulin needs to be discarded at end of month).

Syringes and Needles6

For pen consider use pen needles that are 31or 32 gauge and 5 mm to 8 mm. For vials consider use syringes that are 1.0 cc with ultrafine 5/16" 31-gauge needles. Instruct patient to leave needle in skin for 5 or more seconds after injection completed. Advice to change needle after single use or at least daily.

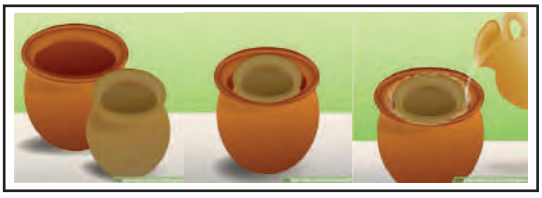
Storage



- *Refrigerate insulin until opened.*
- *Discard after expiration date. Once opened can be kept at room temperature.*
- *Avoid heat.*
- *Replace insulin vial or pen as required per specific insulin package insert.*

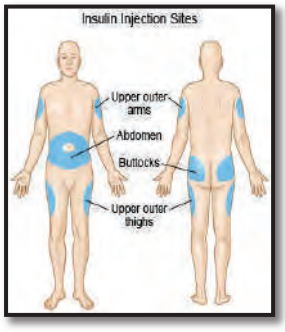
လျှပ်စစ်မီးမရှိသော ဒေသဖြစ်နေပါက

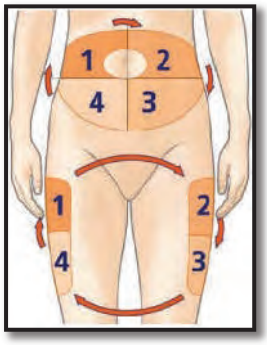
- မြေအိုး ကြီးကြီး ၁လုံး၊ မြေအိုးသေးသေး ၁လုံး ယူပါ။
- အိုးကြီးကြီးထဲကို အိုးသေးသေးထည့်ပါ။
- အိုး ၂ လုံး ကြားထဲကို သဲ ထည့်ပါ။
- သဲထဲကို ရေလောင်းထည့်ပါ။
- အင်ဆူလင် ပုလင်းကို အိုးသေးသေးထဲ ထည့်၍ ဖုံးအုပ်ထားပါ၊



အင်ဆူလင်ထိုးမည့်နေရာများ

- လက်မောင်းအပေါ်ဘက် နောက်ဘက်၊
- ဝမ်းဗိုက်၊
- ပေါင် (ပေါင်အပေါ် ပိုင်းနှင့်ဘေးပိုင်း)
- ကလေးငယ်များတွင် တင်ပါး၌ထိုးနိုင်ပါသည်။





- ဆေးထိုးမည့်နေရာကို ပုံတွင်ပြထားသည့်အတိုင်း ၂ပိုင်း (သို့မဟုတ်) ၄ပိုင်းပိုင်းပါ။
- တစ်ပတ်လျှင်တစ်ပိုင်းစီထိုးပါ။
- နာရီလက်တံ (သို့မဟုတ်) နာရီလက်တံပြောင်းပြန်အတိုင်း လှည့်ထိုးပါ။
- ဆေးတစ်ကြိမ်နှင့် တစ်ကြိမ်ကြား လက်တစ်လုံးခြား (၁ စင်တီမီတာစီ) ခွာထိုးပါ။

Insulin Available in Myanmar

Insulin Type	Conventional	Analogue
Prandial (Insulin R)	**Short acting regular human Insulin** • Actrapid • Wolsulin R • Insunova R • Gensulin R • Maxsulin R	**Rapid Acting** • Novorapid (Aspart)
Basal (Insulin N or G)	**Intermediate acting (NPH) (Insulin N)** • Insulatard • Insunova N • Wolsulin N • Gensulin N • Maxsulin N	**Long acting (Insulin G)** • Glaritus (Glargine) • Insunova G (Glargine) • Levemir (Detemir)
Pre-mixed (Insulin 30/70)	**Combination of short and intermediate acting (30% short + 70% NPH)** • Mixtard 30 • Insunova 30/70 • Wolsulin 30/70 • Gensulin M30 • Maxsulin 30/70 and 50/50	**Combination of rapid acting & protaminated analogue** • Novomix 30 **Combination of Aspart 30% and Degludec 70%** • Ryzodeg

တစ်နေ့တစ်ကြိမ်ထိုးစနစ်	
ဘယ်အချိန်စ	သောက်ဆေး ၃မျိုး (သို့) ၄မျိုးဖြင့် ဆီးချိုမထိန်းနိုင်လျှင်
ဘယ်ဆေး	Insulin N, Insulin G
ဘယ်လိုစ	ညအိပ်ရာ မဝင်မီ ၁၀ ယူနစ်
ဘယ် အဖြေကိုကြည့် ချိန်ညှိ	နံနက်စာ မစားခင် အဖြေ
ဘယ်လိုချိန် (၃ရက်တခါ လိုလျှင်တိုးရန်) (ကျလျှင် တကြိမ်ကျရုံဖြင့် လျှော့ရန်)	၈၀ mg/dl အောက် = ၂ယူနစ်လျော့ ၈၀-၁၃၀ကြား = ယခင်အတိုင်း ဆက်ထိုး ၁၃၀ အထက် = ၂ ယူနစ်တိုး
အမြင့်ဆုံး	၀.၅ ယူနစ်/kg/day

တစ်နေ့နှစ်ကြိမ်ထိုးစနစ်	
ဘယ်အချိန်စ	တစ်နေ့တစ်ကြိမ်ထိုးစနစ်ဖြင့် ဆီးချို မထိန်းနိုင်လျှင်
ဘယ်ဆေး	Insulin ၃၀/၇၀ အရော, Novomix Insulin
ဘယ်လိုစ	မနက်စာ မစားမီ နာရီဝက် ညစာ မစားမီ နာရီဝက်
ဘယ် အဖြေကိုကြည့် ချိန်ညှိ	မနက်အင်ဆူလင် = နေ့လည်စာမစားခင်နှင့် ညနေစာမစားခင် သွေးချိုအဖြေ ညအင်ဆူလင် = ညအိပ်ခါနီးနှင့်နောက်တစ်နေ့ မနက်မစားခင် သွေးချိုအဖြေ
ဘယ်လိုချိန် (၃ရက်တခါ လိုလျှင်တိုးရန်) (ကျလျှင် တကြိမ်ကျရုံဖြင့် လျှော့ရန်)	၈၀ အောက် = ၂ယူနစ်လျော့ ၈၀-၁၃၀ကြား = ယခင်အတိုင်း ဆက်ထိုး ၁၃၀ အထက် = ၂ ယူနစ်တိုး
အမြင့်ဆုံး	သတ်မှတ်ချက်မရှိ

တစ်နေ့လေးကြိမ်ထိုးစနစ်	
ဘယ်အချိန်စ	နေ့ နှစ်ကြိမ်ထိုးစနစ်ဖြင့် ဆီးချို မထိန်းနိုင်လျှင်
ဘယ်ဆေး	Insulin R + Insulin N Novorapid + Insulin G/Detemir
ဘယ်လိုစ	မနက်စာ နေ့လည်စာ ညစာ မစားမီ = Insulin R/ Novorapid ညအိပ်ရာဝင် = Insulin N/Insulin G/Detemir
ဘယ်အဖြေကိုကြည့် ချိန်ညှိ	မနက်အင်ဆူလင်= နေ့လည်စာမစားခင် သွေးချိုအဖြေ နေ့လည်အင်ဆူလင် = ညနေစာမစားခင် သွေးချိုအဖြေ ညအင်ဆူလင် = ညအိပ်ခါနီး သွေးချိုအဖြေ ညအိပ်ခါနီးအင်ဆူလင် = နောက်တစ်နေ့ မနက်မစားခင် သွေးချိုအဖြေ
ဘယ်လိုချိန် (၃ရက်တခါ လိုလျှင်တိုးရန်) (ကျလျှင် တကြိမ်ကျရုံဖြင့် လျှော့ရန်)	၈၀ အောက် = ၂ယူနစ်လျော့ ၈၀-၁၃၀ကြား = ယခင်အတိုင်း ဆက်ထိုး ၁၃၀ အထက် = ၂ ယူနစ်တိုး
အမြင့်ဆုံး	သတ်မှတ်ချက်မရှိ

THE USE OF VARIABLE RATE INTRAVENOUS INSULIN INFUSION (VRIII)

Medical patients[7]	Surgical patients
Absolute Indications 1. NBM more than one missed meal 2. Type 1 diabetes with recurrent vomiting (exclude DKA) 3. Type 1 or 2 diabetes and severe illness needing to achieve good glycaemic control e.g. sepsis **Special circumstances**: ACS, stroke, TPN/enteral feeding/ steroids and pregnancy (seek advice from the diabetes team)	1.Long starvation period (i.e. more than one missed meal) 2.CBG >180mg/dl during fasting or 1 hour before surgery 3.Major surgery (e.g., chest or abdominal cavity, vascular bypass, transplant, spinal or brain surgery requiring general anesthesia, total hip or knee replacement, surgery anticipated to be longer than 4 hours)
Monitoring and Target - Capillary blood glucose (CBG) must be checked every hour until CBG in range (140 ~180 mg/dL) - Avoid hypoglycaemia (CBG < 70 mg/dL) - Limit use to < 24 hours where possible	

Preparation for VRIII	Insulin infusion and Fluid line connect with 3-way connector	
Fluid (10% DW)	**Rate of infusion**	**Potassium mmol/L in 10 % DW**
No concern of fluid overload	**125 ml/hr**	< 3.5 – KCL 20 mmol/500 ml 3.5- 5 – KCL 10 mmol/500 ml > 5 – No additional KCL
Patients with severe heart or renal failure or already on other fluid therapy	Infusion fluid rate **40 ml/hr**	

Suggested Scales for insulin infusion rate[7]			
Capillary Blood Glucose	**Reduced Rate** Units/ hour	**Standard Rate** Units/ hour	**Increased Rate** Units/ hour
	lean or elderly patients or low basal or meal insulin doses (<24 Units/day)	Most of the patients	Steroids, TPN or tube feeding or high basal or meal insulin doses (>100 Units /day)
<70 mg/dl	Inpatient hypoglycaemia policy	Inpatient hypoglycaemia policy	Inpatient hypoglycaemia policy
70 – 110 mg/dl	0	0	0
111 - 140 mg/dl	0.5	1	2
141 - 210 mg/dl	1	2	4
211 - 280 mg/dl	2	4	6
281 - 350 mg/dl	3	5	7
351 - 420 mg/dl	4	6	8
> 420mg/dl	6	8	10
IV Insulin 50U Insulin (regular/short acting) + 50 cc N/S by syringe pump If no syringes pump/ infusion pump - 50U in 500 N/S.i.e. 1Unit insulin in 10 ml			

CBG = capillary blood glucose, NBM = nil by mouth, TDD = Total daily dose, ACS = Acute coronary syndrome, TPN = Total preantral nutrition

Discontinuation of VRIII and Restarting Therapy in Patients with Type 2 Diabetes[7]

- ❖ Ensure the patient is able to eat and drink
- ❖ CBGs are in the range 140 ~180 mg/dL
- ❖ That discontinuation takes place at a mealtime (preferably breakfast or lunch but evening meal is acceptable)

Good Control (HbA1c < 7.5%)

Previously Non-insulin treated patients

Restart at usual dose(s) / time(s)**

Previously on subcutaneous insulin

Previously GLP 1 agonist

Restart at usual dose(s) / time(s)
If pancreatitis is suspected promptly discontinue
If eGFR <30ml/min do not use adjustments may be necessary

Once or twice daily long-acting insulin	Once or Twice daily mixed insulin daily mix insulin	Basal bolus insulin regime
Restart usual dose when it is due. If it is necessary to stop VRIII but the basal insulin is not due for several hours, give half the usual dose of basal insulin.	Restart usual dose of insulin together with a meal (either breakfast or evening meal). If it is necessary to stop VRIII at lunchtime, give half the usual breakfast dose of mixed insulin	Restart usual diabetes treatment together with a meal Restart bolus dose of insulin together with the next meal

****Consideration[7]**
Metformin - should only be recommenced when eGFR is >30 ml/min/1.73 m^3
Insulin secretagogues – can be considered to restart in reduced dose if oral intake reduced
Pioglitazone – review if admitted with heart failure, macular edema or a lower limb fracture following a fall
SGLT-2 inhibitors – review if admitted with uro-genital infection or **diabetic ketoacidosis**
DDP4 inhibitors – review if patient was admitted with suspected pancreatitis
Alpha Glucosidase Inhibitors – review if the patient is getting flatulence or diarrhea

General Principles for Restarting subcutaneous insulin

- ❖ There should always be an overlap between the VRIII and injection of subcutaneous insulin;
- ❖ Do not stop VRIII until at least 30-60 minutes after insulin has been given and patient has eaten
- ❖ The pre-admission dose of insulin may need to be reduced if food intake is likely to be limited or the patient was admitted with low blood sugars
- ❖ **Monitor** - CBG should be checked one hour after discontinuing VRIII and at least 4 times for the next 24 hours, to ensure that there is no rebound hyper- or hypoglycaemia

Suboptimal Control (HbA1c > 7.5%)

Discuss with local diabetes in-patient team. Insulin regime may need adjusting

Step 1 - Calculate the total daily dose Insulin (TDD) using either method A or B

Method A[7]
TDD Insulin = 0.5 x body weight in kg
TDD Insulin = 0.3 x body weight in kg
(Frail elderly patients, CKD stage 4 or 5, severe hepatic failure, newly diagnosed Type 1DM)

OR

Method B[7]
Divide the total dose of insulin administered in last 6 hours of the VRIII by 6 = average hourly dose of insulin
Multiply this by 20 (not 24, to reduce risk of hypoglycaemia)

Step 2 - Use the TDD to convert the patient to either a premixed twice daily insulin regime or basal bolus regime

→ See basal bolus and premixed insulin adjustment

Step 3 - Review response to any new insulin regime prior to discharge

→ Ensure the patient and carers are confident in using the insulin delivery device prior to resuming self-management.
Refer to the inpatient diabetes team for education and support

Perioperative adjustment of insulin[8,9]

Day prior to surgery

Basal insulin - take **80 %** (NPH or Glargine)
Prandial Insulin -Take as usual if patient is eating
Premixed insulin- Take as usual

Day of Surgery

AM surgery
Prandial Insulin -- Omit
Basal Insulin
Once daily-Morning injection –
Take **50 %** of the dose for **NPH**
Take **80 %** of the dose for **glargine or detemir**
Once daily-Evening injection – Take as usual
Premixed Insulin --
Morning dose – Omit
Evening dose - Take as usual if evening meal is allowed to eat

PM surgery
Prandial Insulin - Give if patient is allowed to eat. Omit when fasting start.
Basal Insulin
Once daily-Morning injection–
Take **50 %** of the dose for **NPH**
Take **80 %** of the dose for **glargine or detemir**
Once daily-Evening - If surgery is not finished
Take 50 % of the dose for NPH
Take 80 % of the dose for glargine or detemir
If surgery is finished -- Take as usual
Premixed Insulin --
Morning dose – 50 % reduction
Evening dose - unchanged if evening meal is allowed / omit if surgery is not finished.

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MYANMAR GUIDELINE ON
GLYCEMIC MANAGEMENT OF TYPE 2 DIABETES MELLITUS
2024
Management of Acute Complications of Diabetes

4. Management of acute complications of Diabetes

Acute Complications of Diabetes

1. Diabetic Ketoacidosis (DKA)
2. HHS
3. Hypoglycemia

1. Diabetic Ketoacidosis (DKA)

Diagnostic criteria for DKA

(all three of the following must be present)

1. D (Diabetes) - Blood glucose >11 mmol/L (>200 mg/dL) or known diabetes mellitus

2. K (Ketone) - Ketonemia > 3.0 mmol/L or significant ketonuria (>2+ and above on standard urine sticks)

3. A (Acidosis) - Bicarbonate (HCO_3^-) < 15 mmol/L and/or venous pH < 7.3

A. History

1. Classic symptoms – polydipsia, polyuria, and weight loss

2. Vomiting / abdominal pain

3. Increased, difficult, or deep respirations

4. Symptoms of infection

B. Physical examination

1. Vital signs
2. Hydration status / peripheral perfusion / hypovolemic shock
3. Acetone – fruity breath and / or Kussmaul respirations
4. Neurologic status
5. Signs of infection

C. Investigations

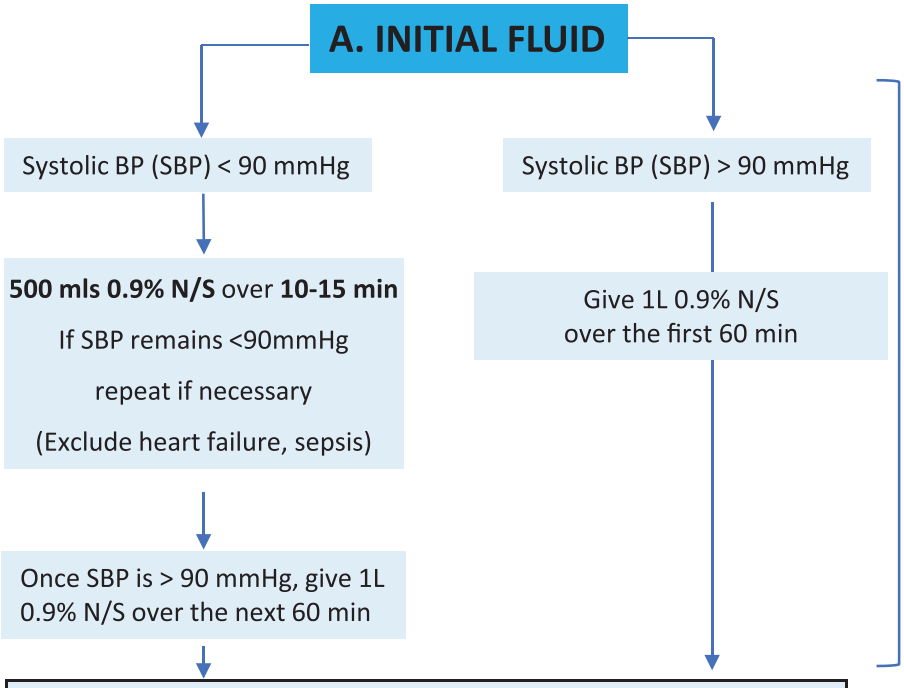
- Capillary and laboratory glucose
- Urinary and blood ketone
- U&E and FBC
- Blood cultures
- ECG
- CXR (Chest X Ray)
- MSU (Mid-stream sample of Urine)

D. Treatment Principles

- Correction of dehydration
- Correction of hyperglycemia
- Correction electrolyte imbalances
- Identification of comorbid precipitating events

Key Points in Management of DKA

- **Start IV fluid before insulin therapy**
- **Potassium level should be > 3.5 mmol/L before initiation of insulin therapy**
- **Initiate continuous Fixed rate intravenous insulin infusion FRIII (0.1 unit/kg/hr),** Measure bedside glucose every 1 hour to adjust the insulin infusion rate.
- **Avoid hypoglycemia during insulin infusion by giving dextrose or reduction of insulin infusion rate until DKA is resolved.**
- **Transition to SC insulin only when DKA resolution is established.**



Fluid replacement rates	
Fluid	**Volume**
0.9% NaCl 1 L	1,000 ml over first hour
0.9% NaCl 1 L with KCl	1,000 ml 2-hourly x 2
0.9% NaCl 1 L with KCl	1,000 ml 4-hourly x 2
Add 10% glucose 125ml/hr if blood glucose < 14 mmol/L (250 mg/dL)	

60 minutes
to
6 hours

B. POTASSIUM REPLACEMENT

K^+ level in first 24h (mmol/L)	KCL in 500 ml of N/S
> 5.5	Nil
3.5 – 5.5	20 mmol in 500 ml
< 3.5	Additional K+ needed: either through increased infusion rate or use of concentrated potassium infusion

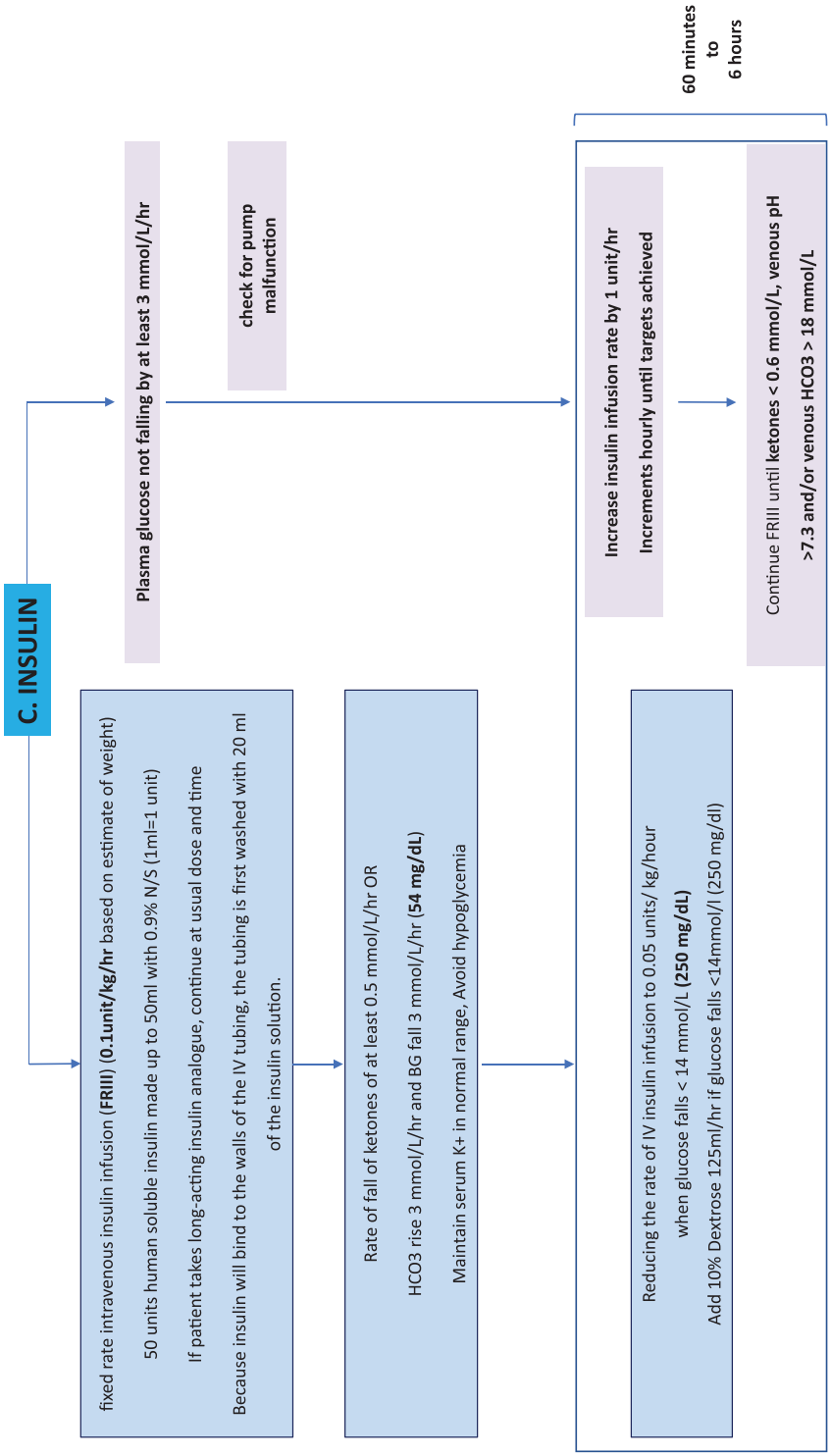
- Serum K+ is maintained between 4.0 – 5.5 mmol/L and checked serum K+ 12 hrly.
- If serum potassium cannot be measured in time, add KCl 20 mmol from third bottle of 500 ml N/S during fluid replacement.

- If serum electrolyte cannot be checked hourly, it should be checked at 6 hours
- If serum electrolyte cannot be checked at 6 hours, it should be checked at 12 hours
- Blood or urine ketones, electrolytes, and venous pH –12 ~24 hours

Metabolic targets

- Increase venous HCO3 - 3 mmol/L/hr
- Reduction in blood ketone – 0.5 mmol/L/hr
- Reduction in capillary blood glucose – 3 mmol/L/hr (55 mg/dL)
- Maintain serum K+ between 4.0 – 5.5 mmol/L
- **Target BG = 180-250 mg/dl (10-14 mmol/l) until ketosis has cleared**

- Continue IV fluid replacement if patient is not eating and drinking
- Continue to treat precipitating factors
- When DKA resolved,
  - If the person is not eating or drinking, move to (**VRII**I)
  - If the person is **able to eat and drink**, transition to subcutaneous insulin
- subcutaneous insulin injection can be initiated with overlap of **at least 1 hour**


C. INSULIN
fixed rate intravenous insulin infusion (FRIII) (0.1unit/kg/hr based on estimate of weight)
50 units human soluble insulin made up to 50ml with 0.9% N/S (1ml=1 unit)
If patient takes long-acting insulin analogue, continue at usual dose and time
Because insulin will bind to the walls of the IV tubing, the tubing is first washed with 20 ml of the insulin solution.
Rate of fall of ketones of at least 0.5 mmol/L/hr OR
HCO3 rise 3 mmol/L/hr and BG fall 3 mmol/L/hr (54 mg/dL)
Maintain serum K+ in normal range, Avoid hypoglycemia
Plasma glucose not falling by at least 3 mmol/L/hr
check for pump malfunction
60 minutes to 6 hours
Increase insulin infusion rate by 1 unit/hr
Increments hourly until targets achieved
Reducing the rate of IV insulin infusion to 0.05 units/ kg/hour when glucose falls < 14 mmol/L (250 mg/dL)
Add 10% Dextrose 125ml/hr if glucose falls <14mmol/l (250 mg/dl)
Continue FRIII until ketones < 0.6 mmol/L, venous pH >7.3 and/or venous HCO3 > 18 mmol/L

Metabolic targets

- Increase venous HCO3 - 3 mmol/L/hr
- Reduction in blood ketone – 0.5 mmol/L/hr
- Reduction in capillary blood glucose – 3 mmol/L/hr (55 mg/dL)
- Maintain serum K+ between 4.0 – 5.5 mmol/L
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- Continue IV fluid replacement if patient is not eating and drinking
- Continue to treat precipitating factors
- When DKA resolved,
  - If the person is not eating or drinking, move to (**VRII**l)
  - If the person is **able to eat and drink**, transition to subcutaneous insulin
- subcutaneous insulin injection can be initiated with overlap of **at least 1 hour**

Criteria for resolution of DKA

- Ketones <0.3 mmol/L
- pH > 7.3
- Venous HCO3 – >18 mmol/L

Use of intravenous bicarbonate therapy ***is routinely not recommended*** (**SE**--cerebral oedema and delay in resolution of ketosis)

may be considered in patients with pH < 7.0 (or) HCO3<10 (or) PCO2 <12**r**

Special consideration

Euglycaemic DKA

- This is the development of DKA in people known to have diabetes but where the glucose is normal, or not particularly raised.
- **This condition is treated in exactly the same way as hyperglycemic DKA.**
  1) Initiate glucose 10% straight away at 125 ml/hr because the glucose is <14 mmol/L
  2) Begin with 0.1units/kg/hr insulin rate
  3) If glucose falling despite 10% glucose reduce to 0.05 units/kg/hr to avoid hypoglycemia
- With the widespread use of the sodium-glucose cotransporter (SGLT) inhibitor class of drugs (e.g. dapagliflozin, canagliflozin, empagliflozin) people with type 2 diabetes has highlighted the importance of using pH and ketones (rather than the older 'glucose-centric' care) to guide the diagnosis and management.
- This is because of the risk of developing euglycaemic DKA with these agents.
- If DKA occurs with SGLT inhibitor use, they should be stopped.
- Whether the drugs should be restarted once the individual has recovered should be discussed with the diabetes team.

Hyperglycemic Hyperosmolar State

Definition

- Hypovalaemia
- Marked hyperglycemia RBS ≥ 540 mg% (≥ 30 mmol/L)
- Osmolality ≥ 320 mosmol/kg (Osmolality = 2Na + Glucose + Urea)
- No significant ketonaemia (Blood ketone ≤ 3mmol/L)
- Without significant Acidosis (pH ≥7.3 and blood or serum bicarbonate ≥ 15 mmol/L

Estimated fluid loss – 100 - 220 ml/kg (6-13 L for 60 kg)

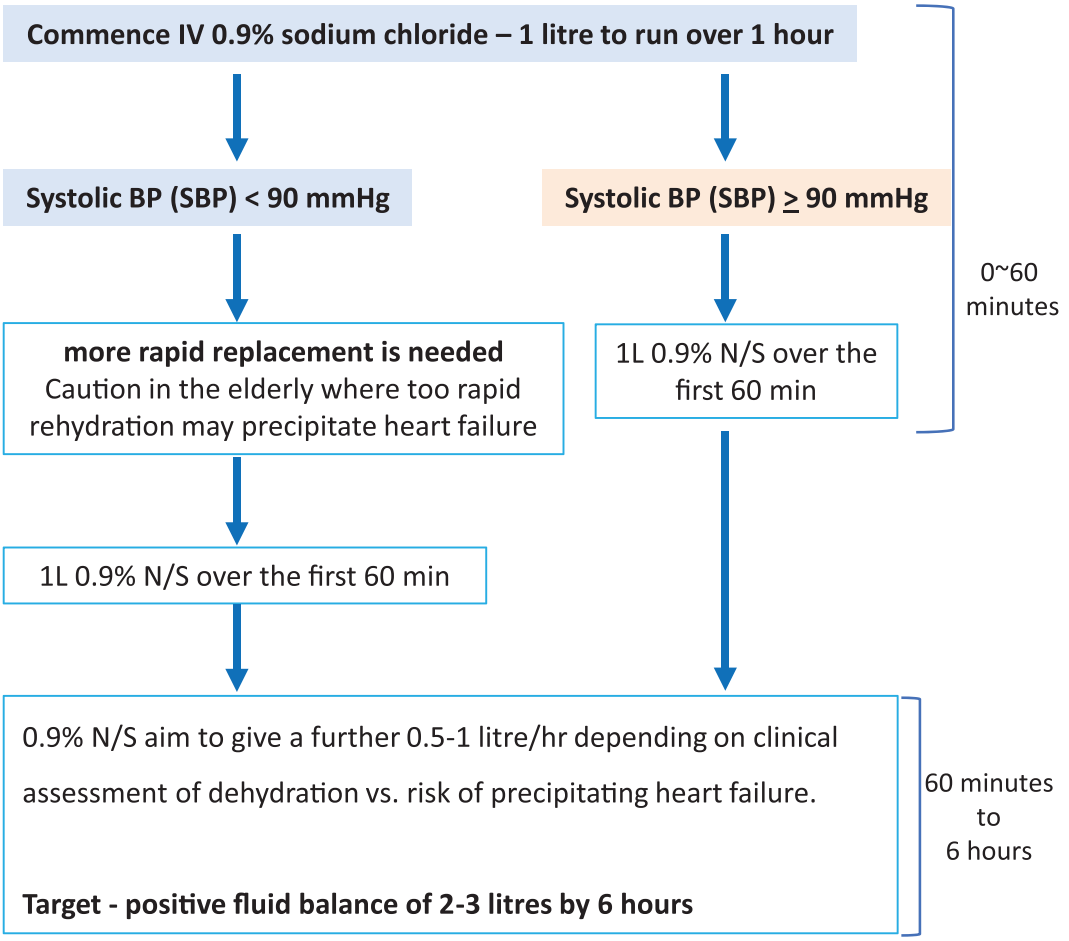
Fluid replacement - 50 % in first 12 hours, 50 % in second 12 hours

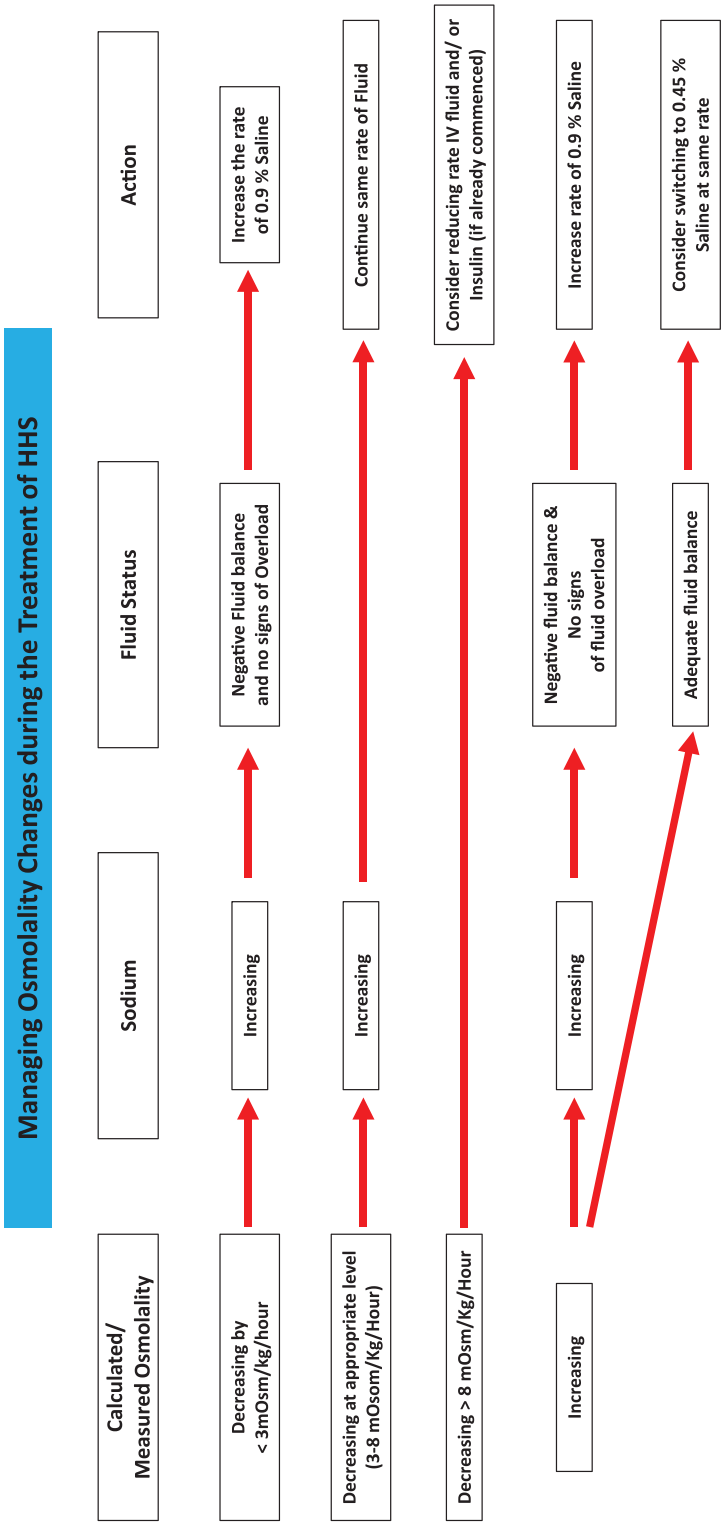
Management

General	Goals of Treatment
1. **Investigations** CBC, Urine RE, ECG,Urine C & S, Blood C & S, CRP (if infection is suspected) **2. Intake/output chart by staff** (catheterization if necessary)	**Normalize the osmolality** • replace fluid and electrolyte losses • normalize blood glucose **Prevention of** ▪ arterial or venous thrombosis ▪ other potential complications e.g. cerebral oedema/central pontine myelinolysis/osmotic demyelination syndrome ▪ foot ulceration

Fluid replacement and changes in osmolality

Initial fluid replacement




Managing Osmolality Changes during the Treatment of HHS
Calculated/ Measured Osmolality
Sodium
Fluid Status
Action
Decreasing by < 3mOsm/kg/hour
Increasing
Negative Fluid balance and no signs of Overload
Increase the rate of 0.9 % Saline
Decreasing at appropriate level (3-8 mOsom/kg/Hour)
Increasing
Continue same rate of Fluid
Decreasing > 8 mOsm/Kg/Hour
Consider reducing rate IV fluid and/ or Insulin (if already commenced)
Increasing
Increasing
Negative fluid balance & No signs of fluid overload
Increase rate of 0.9 % Saline
Adequate fluid balance
Consider switching to 0.45 % Saline at same rate

Insulin Therapy

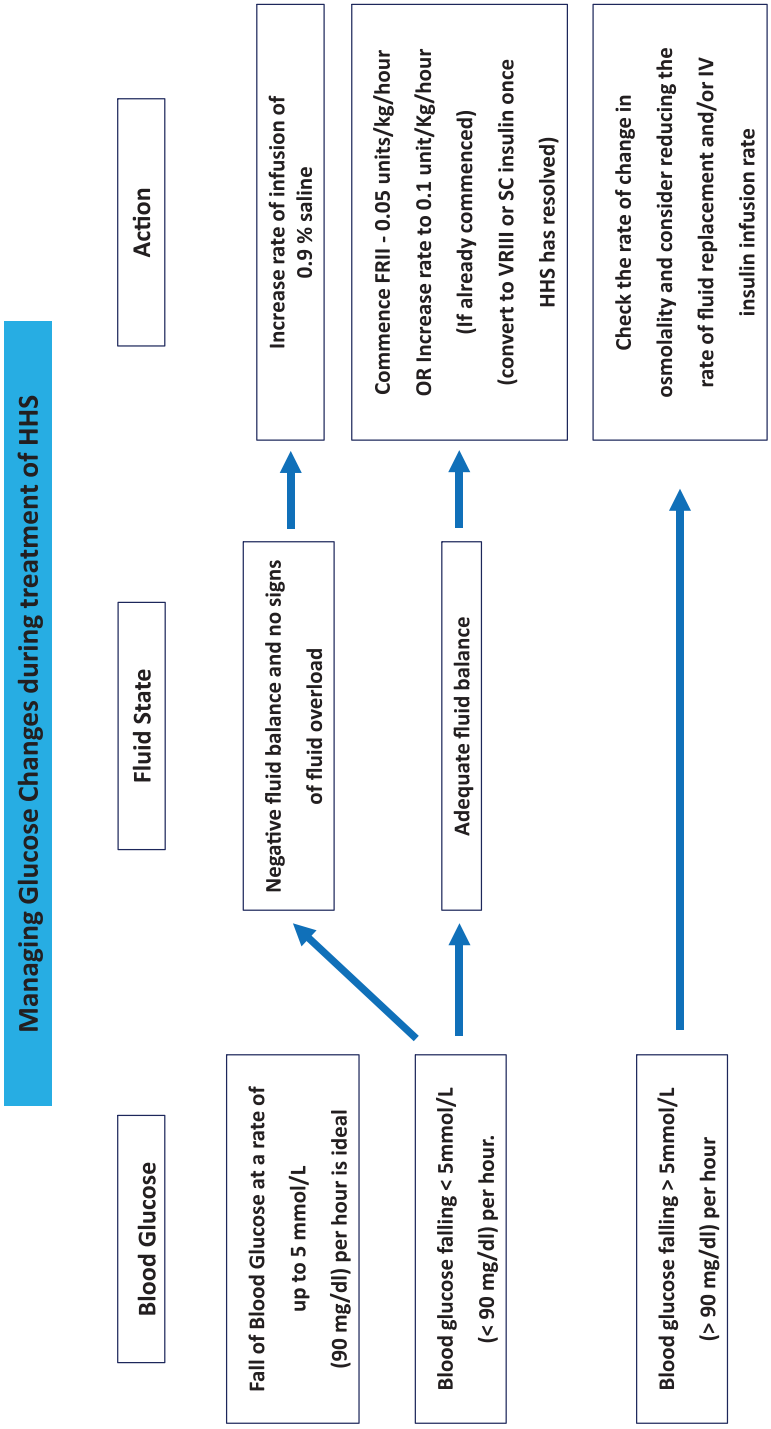
- ONLY START IV INSULIN once fluid replacement is adequate and glucose concentrations have plateaued
- Starting an IV insulin infusion too early could result in circulatory collapse
- Fixed rate insulin infusion (**FRIII at 0.05 units/kg/hr**)
- increase rate to 0.1 units/kg/hr if glucose concentrations are not falling

Insulin Infusion (FRIII)

If there is HHS and ketonaemia (Blood ketone-3β hydroxybutyrate > 1.0- ≤ 3.0 mmol/L or Urine ketones < 2 +and not acidotic (Venous pH > 7.3 and bicarbonate > 15.0 mmol/L)	If there is significant ketonaemia (3ß-hydroxybutyrate>3.0 mmol/L) or ketonuria (≥ 2+) with a pH <7.3 And bicarbonate <15 mmol/L (i.e. mixed DKA and HHS)
↓	↓
Use 0.05 units/kg/hr	Use the DKA guideline at 0.1 units/kg/hr

Monitoring

- Blood glucose- Monitor hourly first 6- 12 hours and then 2 hourly according to clinical response
- Electrolytes and calculated osmolality- At least daily , if possible 12 Hourly
- Monitor Vital Signs- BP HR and pulse oximetry according to clinical status
- Consider continuous cardiac monitoring if necessary


Managing Glucose Changes during treatment of HHS
Blood Glucose
Fluid State
Action
Fall of Blood Glucose at a rate of up to 5 mmol/L (90 mg/dl) per hour is ideal
Blood glucose falling < 5mmol/L (< 90 mg/dl) per hour.
Blood glucose falling > 5mmol/L (> 90 mg/dl) per hour
Negative fluid balance and no signs of fluid overload
Adequate fluid balance
Increase rate of infusion of 0.9 % saline
Commence FRII - 0.05 units/kg/hour OR Increase rate to 0.1 unit/Kg/hour (If already commenced) (convert to VRIII or SC insulin once HHS has resolved)
Check the rate of change in osmolality and consider reducing the rate of fluid replacement and/or IV insulin infusion rate

Clinical and biochemical parameters

Continue IV fluid replacement positive balance of 3-6 liters by 12 hours

Avoid hypoglycemia

Aim to keep BG 10-15 mmol/L (180-270 mg/dl) in first 24 hours

If BG falls < 14 mmol/L(< 250 mg/dl) commence 5% or 10% glucose at 125 ml/hr AND CONTINUE 0.9% sodium chloride solution

Blood glucose hourly, sodium & calculated osmolality daily, if possible 12 hourly

6~12 hour

Continue IV fluid replacement to achieve remaining replacement of estimated fluid losses within next 12 hrs.

Continue IV insulin +/- 5 or 10% glucose - to maintain BG 10-15 mmol/L(180-270 mg/dl)

Adjust insulin infusion rate hourly by 1 unit/hr increments or decrements

12~24 hour

Continue IV fluids until eating and drinking normally

VRIII if not eating and drinking

Convert to appropriate subcutaneous insulin regime when biochemically stable and can eat will

Encourage early mobilization

24 hour to Day 3

Potassium replacement

➢ This is the same as DKA.

Anticoagulation

➢ All patients should receive prophylactic low molecular weight heparin for the full duration of admission unless contraindicated.

Aim of Treatment	Criteria for Resolution of HHS
▪ Rate of fall of osmolality - 3-8 mOsmol/kg/hr ▪ Target blood sugar - 10-15 mmol/L (180 - 270 mg/dl) in first 24 hours ▪ Improvement of clinical status and replacement of estimated fluid loss in 24 hour ▪ Avoid hypoglycemia and hypokalemia ▪ Prevent VTE, osmotic demyelination, fluid overload, Foot ulceration	▪ Clinical & Cognitive status is back to precomorbid state ▪ Osmolality < 300 mOsm/kg ▪ Hypovolaemia has been corrected (Urine Output ≥ 0.5ml/kg/hr) ▪ Blood Glucose < 15 mmol/L(< 270 mg/dl)

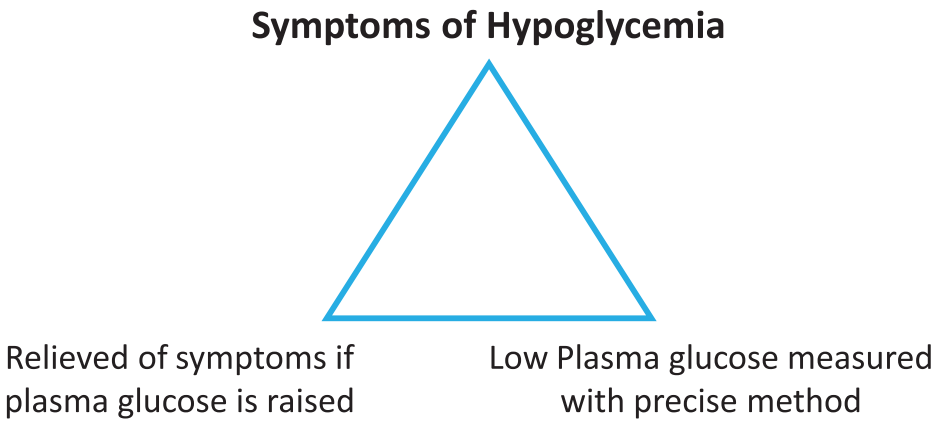
Before D/C	After D/C
• Diabetes education must be given to all patients • Arrange follow-up with diabetes team	• Most people should go home on subcutaneous insulin • For those with previously undiagnosed diabetes or well controlled on oral agents, switching from insulin to the appropriate oral hypoglycemic agent should be considered.

Hypoglycemia

Classification of Hypoglycemia

- **Level 1 Hypoglycemia** – Glucose < 70mg/dl (<3.9 mmol/l) and ≥ 54 mg/dl (≥ 3.0 mmol/l)
- **Level 2 Hypoglycemia** – Glucose < 54 mg/dl (<3.0 mmol/l)
- **Level 3 Hypoglycemia** – A severe event characterized by altered mental and /or physical status requiring assistance for treatment of Hypoglycemia, irrespective of Glucose level

Whipple Triad



Management of Hypoglycemia

Mild

Adults who are conscious, orientated and able to swallow

1. Check ABCDE, stop IV insulin (if running)
2. Give 15-20g of quick acting carbohydrate, such as 3-5 heaped teaspoons of sugar or 150-200ml pure fruit juice
3. Test blood glucose level after 10-15 min and if still <4.0mmol/L (< 70 mg/dl) repeat treatment as above up to 3 times.
4. If still hypoglycemic, call doctor and consider IV dextrose or IM glucagon as per "severe" pathway

Moderate

Patient conscious and able to swallow, but confused, disorientated or aggressive

1. Check ABCDE, stop IV insulin (if running)
2. If capable and cooperative, treat as for mild hypoglycemia.
3. If not capable and uncooperative, treat as severe hypoglycemia.
4. Test blood glucose level after 10-15 minutes and if still < 4.0mmol/L(< 70 mg/dl)repeat as above up to 3 times.
5. If still hypoglycemic, call doctor and consider IV dextrose or IM glucagon as per "severe" pathway

Severe

Patient unconscious/fitting or very aggressive or nil by mouth (NBM)

1. Check ABCDE, stop IV insulin, request medical support urgently.
2. Give 200ml 10% dextrose over 15 minutes or 2 ampules (40ml) of 50% glucose (risk of extravasation injury)
3. Recheck glucose after 10 – 15 minutes and if still < 4.0mmol/L (< 70 mg/dl), repeat treatment as above
4. If IV access is not possible use 1mg Glucagon IM

Check glucose after 10-15 minutes. Once blood glucose level are now > 4.0 mmol/L (> 70 mg/dl) or above:
- Give 20g of long acting carbohydrate e.g. two biscuits, slice of bread or net carbohydrate containing meal.
- Give 40 g if IM glucagon has been used.
- For patients with enteral feeding tube, give carbohydrate containing fluid e.g. 50-70 ml Fortijuice or 3-5 heaped teaspoons of sugar in water via enteral tube.

If glucose is 4.0mmol/L (70 mg/dl) or above, follow up treatment as described on the above.
If NBM, once glucose > 4.0mmol/L (> 70 mg/dl) give 10% glucose infusion at 100ml/hr until no longer NBM or reviewed by doctor

DO NOT omit subsequent insulin doses.

- Continue regular capillary blood glucose monitoring for 24-48 hours.
- Review insulin and/or oral hypoglycemic doses.
- If previously on IV insulin, would generally consider restarting insulin once blood glucose >4.0 mmmol/L (> 70 mg/dl) but may require review of regimen.
- Give hypoglycemia education and refer to inpatient diabetes team.

Glucagon may take up to 15 minutes to work and may be ineffective in treating hypoglycemia in undernourished patients, in severe liver disease, sulfonylurea induced hypoglycemia and in repeated hypoglycemia.

When hypoglycemia has been successfully treated

- Replenish “hypo boxes”
- Identify the risk factor
- Take measures to avoid hypoglycemia in the future.
- It may be safe to omit a meal time bolus dose of rapid acting insulin if the patient is declining food and had their usual basal insulin.
- Dose adjustment

Examples of Hypo Box

- Copy of hypoglycemia algorithm (laminated and attached to inside of lid)
- 2x 200ml carton fruit juice
- 2 x packets of Glucose powder
- 1x mini pack of biscuits (source of long acting carbohydrate)
- 10% Glucose IV solution

Reference

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3. Glycemic Targets: Standards of Medical Care in Diabetes—2022
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2024
Glycemic Management of Diabetes in Pregancy

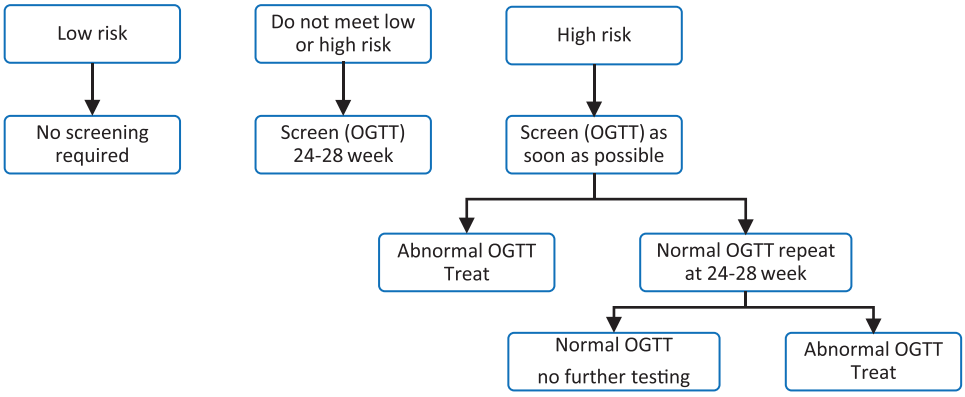
Glycemic Management of Diabetes in Pregnancy

(1) Diagnosis of Gestational diabetes

75-g OGTT (75 g anhydrous glucose powder or 82.5g monohydrous glucose) one-step strategy is recommended[1,2]

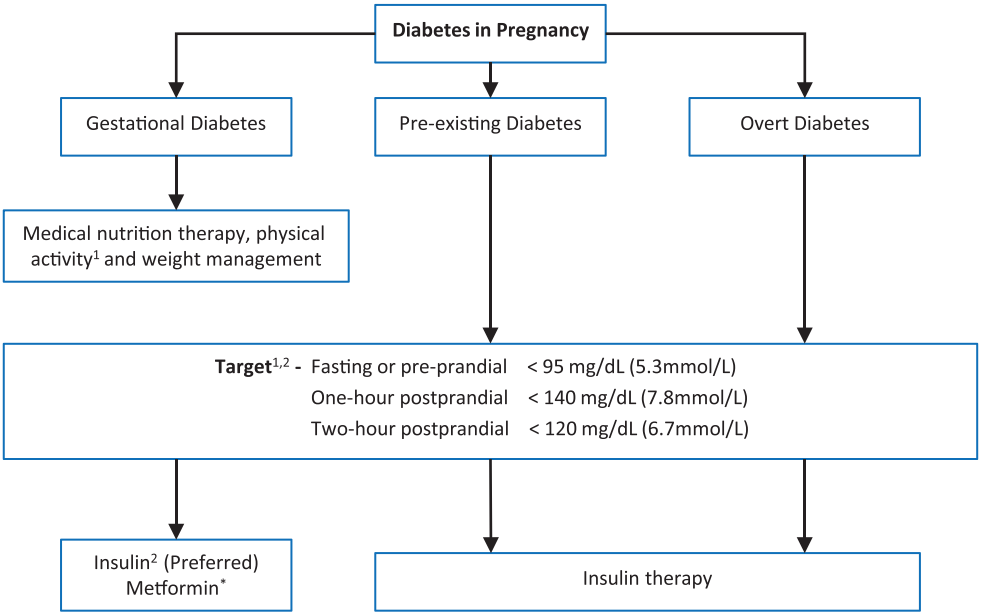
The diagnosis of GDM is made when *any of the following* plasma glucose values are met or exceeded:			
Diagnosis[1,2]	Fasting	1 h	2 h
GDM	≥92mg/dl (5.1mmol/L)	≥ 180mg/dl (10 mmol/L)	≥ 153mg/dl (8.5mmol/L)
Overt DM (Type 1 or 2)	Fasting plasma glucose value ≥ 126 mg/dl (7.0 mmol/L) and/or 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) and/or random plasma glucose value ≥ 200 mg/dl (11.1 mmol/l) in the presence of symptoms, and/or HbA1c ≥ 6.5% (48 mmol/mol)		
Measurement of Urine glucose is not recommended			

Timing of OGTT[3]



High risk (one or more risk factors)	Intermediate risk	Low risk (all must be present)
• BMI above 30 kg/m^2 • Previous macrosomic baby weight ≥ 4 kg • Previous gestational diabetes • First-degree relative with diabetes • Family origin with a high prevalence of diabetes (South Asian) • Poor Obstetric outcome (congenital anomalies, history of early neonatal death, unexplained fetal death, miscarriages)	Neither High or low risk	Age <25 years AND • Weight normal before pregnancy AND • No history of abnormal glucose metabolism AND • No history of poor obstetric outcome

(2) Glycemic Management during Pregnancy



*Metformin should not be used as first-line agent, as it crosses placenta[2]

Metformin maximum dose 1.5 g/ day[4]

Need to discuss with patient for possible side effects

Metformin should not be used in women with hypertension or preeclampsia or at risk for intrauterine growth restriction[5]

Immediate Insulin therapy is recommended if[4]

(a) fasting plasma glucose level ≥ 126 mg/dL (7.0 mmol/L) at diagnosis

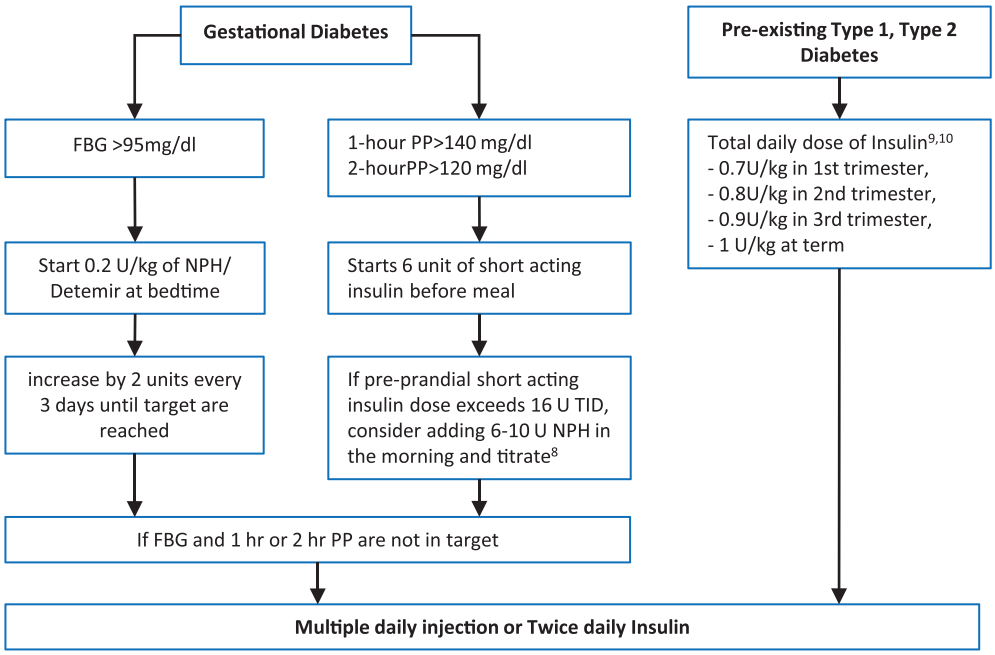
(b) who have a fasting plasma glucose level of between 108~124.2 mg/dL (6.0 and 6.9 mmol/L) if there are complications such as macrosomia or hydramnios

Overt diabetes in pregnancy - hyperglycemia first recognized during pregnancy which meets the diagnostic threshold of diabetes in non-pregnant adults.

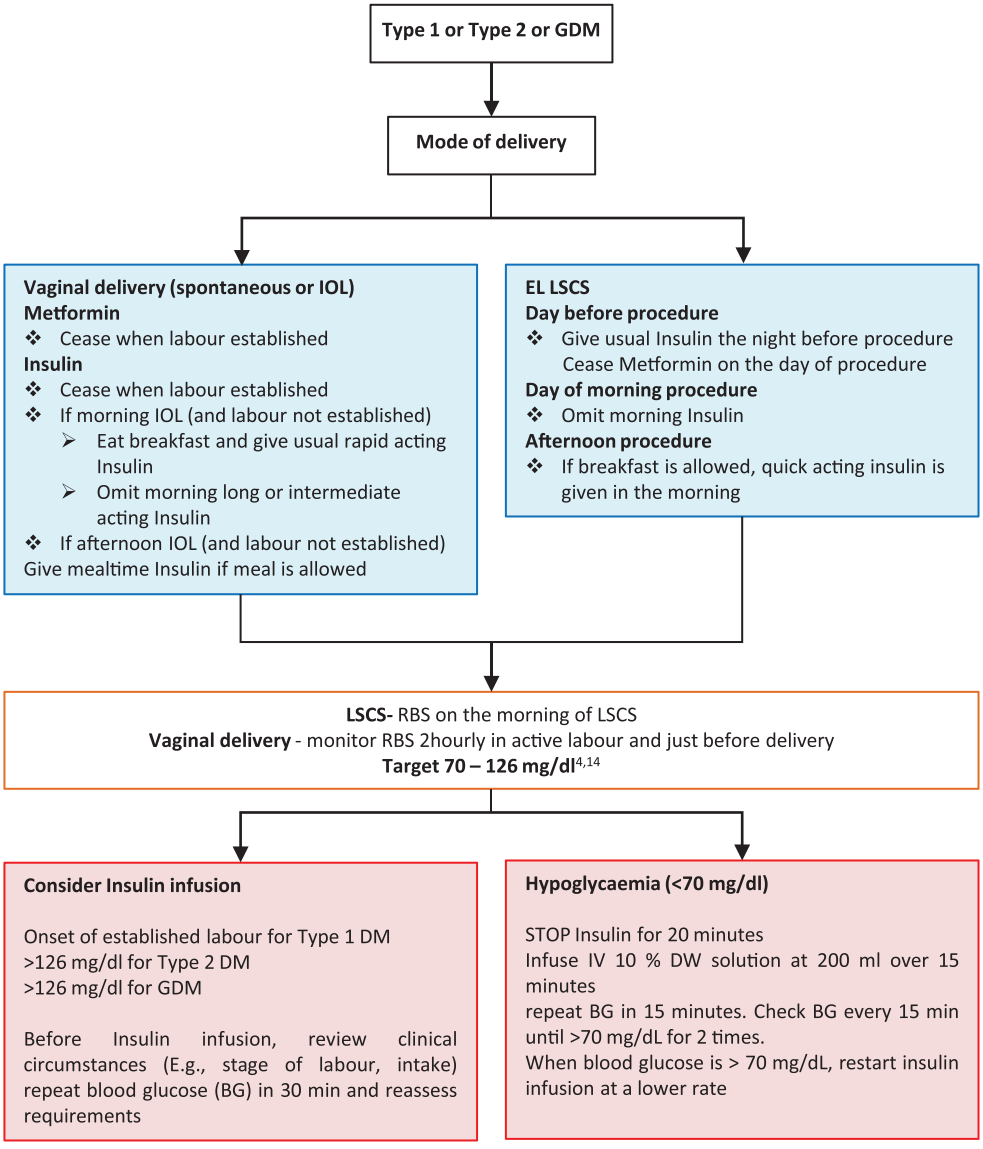
Insulin use in Pregnancy		
Insulin Types	**Category**	**Recommendation**
NPH insulin	Category B	first choice for long-acting insulin
Glargine	Category C	(AACE, Endo), can continue (NICE 2015)
Detemir	Category B	FDA approved
Lispro and Aspart	Category B	Lifestyle flexibility, greater patient satisfaction, better postprandial blood glucose control
Regular insulin	Category B	Comparable to rapid acting insulin

- When the glycemic controls need to initiate insulin, multiple daily injection is the best insulin regimen[4,7]
- Twice daily insulin injection can be given (refer to twice daily Insulin)
- Preference should be given to rapid acting insulin analogs to treat postprandial hyperglycemia in pregnant subjects. Regular insulin is acceptable when analogs are not available[7]
- If antenatal corticosteroid therapy is required, Insulin dose should be adjusted accordingly.

Insulin Dose in Pregnancy



(3) Intrapartum Management

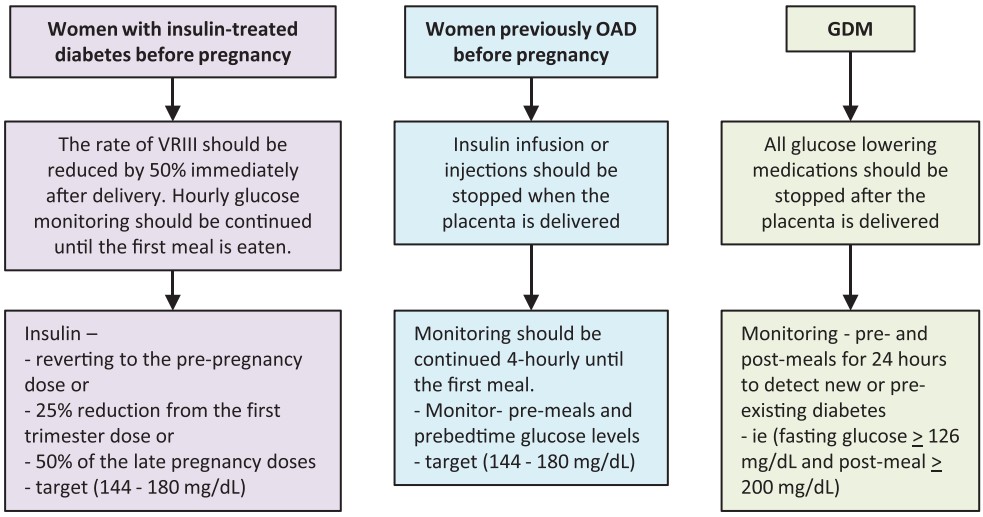


Intravenous Insulin Prescription and Fluid Protocol for Pregnancy and Diabetes

Check blood glucose every hour while on insulin drip.	**Begin IV fluids** –5% DNS - 125 ml/hr [11,12] - 5% DNS 50 ml/hr (in Pre-eclampsia)	
	Intra-partum	**Post-partum**
	50 units Regular human insulin in 50 ml NS (1ml = 1unit insulin) ‡	
Blood glucose (mg/dL)	Units of insulin in ml/hr [9]	Units of Insulin in ml/hr
<70 (treat for hypoglycemia)	0	0
71-90	0.5 ml/hr	0
91-110	1 ml/hr	0.5 ml/hr
111-130	2 ml/hr	1 ml/hr
131-150	3 ml/hr	1.5 ml/hr
151-170	4 ml/hr	2 ml/hr
171-190	5 ml/hr	2.5 ml/hr
>190	Consult Endocrinologist, check for ketone	

‡If syringe pump or infusion pump is not available, 10 units of soluble insulin in N/S 500ml (1 unit=50 ml) can be prepared for insulin infusion.

(4) Postpartum recommendations for women with diabetes[11]



OGTT is recommended at 4–12 weeks postpartum using nonpregnancy criteria.
Women with a history of gestational diabetes mellitus found to have prediabetes should receive intensive lifestyle interventions and/or metformin to prevent diabetes.
GDM is associated with an increased lifetime maternal risk for diabetes and women should also be tested every 1–3 years if postpartum OGTT is normal.

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MYANMAR GUIDELINE ON

GLYCEMIC MANAGEMENT OF TYPE 2 DIABETES MELLITUS

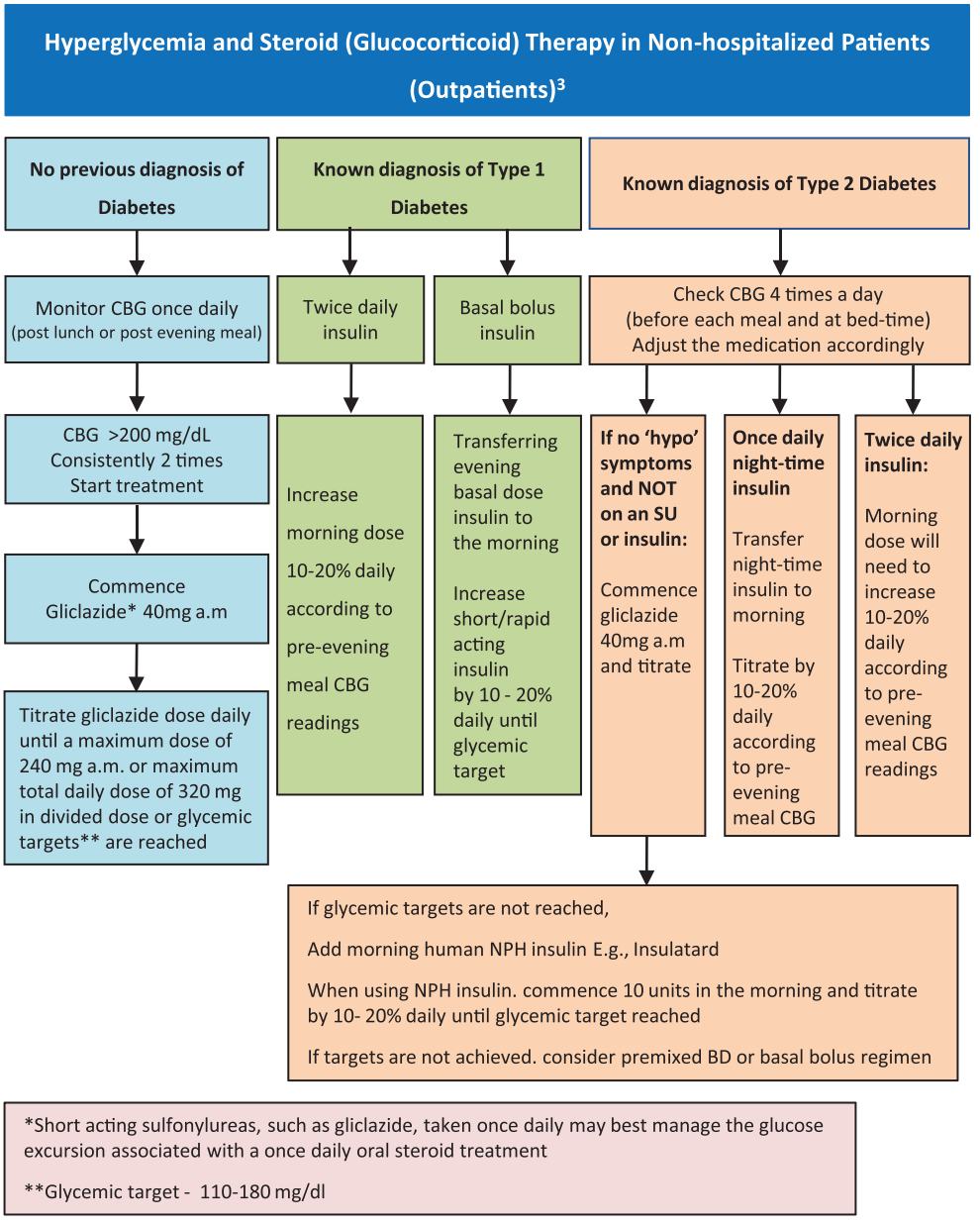
2024

Management of Hyperglycemia and Steroid (Glucocorticoid) Therapy

Management of Hyperglycemia and Steroid (Glucocorticoid) Therapy

Introduction	
❖ Glucocorticoid induced hyperglycemia (SIHG) and diabetes are related to the duration of time on steroids, the potency of the drug used and the doses given.	
Definition[3]	
Steroid induced diabetes	A rise in glucose related to steroid therapy occurring in people **without** a known diagnosis of diabetes is termed **steroid induced diabetes**. This may or may not resolve when the steroids are withdrawn
Steroid induced hyperglycemia	The use of steroid treatment in people **with pre-existing diabetes** will undoubtedly result in worsening glucose control; this may be termed **steroid induced hyperglycemia**. This warrants temporary additional and more active glycemic management.
Diagnostic criteria for steroid induced diabetes[1]	
Do not differ from other types of diabetes and include a confirmed 1. Fasting blood glucose ≥7 mmol/L (≥126 mg/dL) 2. Glucose level of ≥11.1 mmol/L (≥200 mg/dL) at 2 h following ingestion of 75 g glucose in an oral glucose tolerance test (OGTT), 3. HbA1c ≥6.5% (≥48 mmol/mol) or 4. Random blood glucose ≥11.1 mmol/L (≥200 mg/dl) with classic symptoms of hyperglycemia	

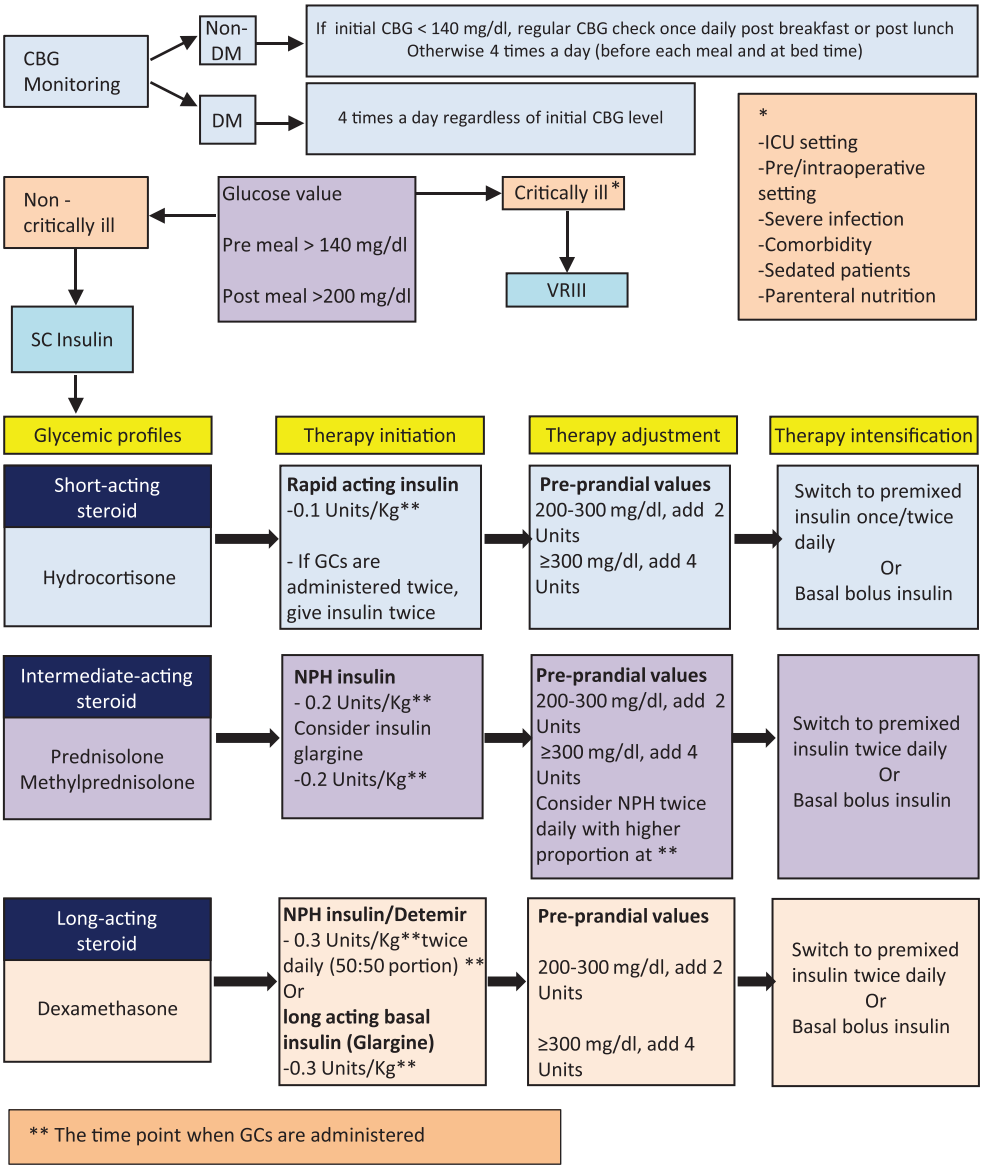
Management of Hyperglycemia in People Taking Steroids



*Short acting sulfonylureas, such as gliclazide, taken once daily may best manage the glucose excursion associated with a once daily oral steroid treatment

**Glycemic target - 110-180 mg/dl

Hyperglycaemia and Steroid (Glucocorticoid) Therapy in Hospitalized Patients (Inpatients)[1]



Duration of action and equivalent doses of steroid[3]

Steroid	Potency (equivalent doses)	Duration of action (half-life, in hours)
Hydrocortisone	20 mg	8
Prednisolone	5 mg	16-36
Methylprednisolone	4 mg	18-40
Dexamethasone	0.75 mg	36-54

Calculation of initial dose of insulin in steroid induced hyperglycemia by weight-based method[7]

- 0.1 Units/kg for every 10 mg of prednisolone or 1.5 mg of dexamethasone up to a maximum of 0.4 Units/kg
- Single dose in the morning together with once daily prednisolone
- Two divided doses for twice daily prednisolone or dexamethasone
- Patients already receiving insulin at home should add the weight-based total to their normal basal insulin dose.

Prednisolone dose (mg/day)	Dexamethasone dose (mg/day)	Insulin dose (NPH/Glargine) (units/kg)
10	1.5	0.1
20	3	0.2
30	4.5	0.3
≥40	≥6	0.4 (maximum)

Eg: For 50 kg patient, taking prednisolone 40 mg (= dexamethasone 6 mg)
0.4 × 50 kg = 20 Units NPH OD or 10 Units NPH BD

Hospital Discharge Plan and Post Hospital Discharge Management[3]

Discharge Plan[3]	
Tail off steroid at home (5mg/week)	• Reduction of insulin dose 20-25 % per week or • A reduction of 40 mg of gliclazide per week • Continue CBG monitoring (once daily in the late afternoon or evening) post discharge until normoglycemia return or do HbA1c. • If CBG back to normoglycemia before discharge, CBG monitoring not necessary
Post Hospital Discharge[3]	
Post discharge CBG monitoring	• If the steroid dose remains above 5mg prednisolone or equivalent, for a protracted period, and the patient is insulin treated then the blood glucose should be checked at late afternoon or evening and prior to driving
Screening of DM post discharge	• HbA1c as a screening tool should be delayed until 3 months following steroid cessation • FBS or OGTT may be advantageous if a diagnosis of diabetes is clinically suspected prior to 3 months elapsing

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