

CHILD WITH REVERSIBLE DIABETES

Dr D Nagarjuna

DNB Pediatrics post graduate

Mehta Hospital, Chennai

Clinical History

- Miss M – 7 year 8 months old female child – A case of reflux nephropathy
- Chronic tubulo interstitial disease – developed chronic kidney disease stage V
- Underwent renal transplantation (Allograft from mother) in December 2012
- Post operatively she was started on triple immunosuppressive therapy with – Tacrolimus 1.5 mg twice a day, MMF 360 mg BD and Prednisolone PO 15mg/day) and later continued with tacrolimus and prednisolone

Clinical History

- On follow-up, she was being monitored for development of hyperglycemia
- 3rd month after transplantation (April 2014) - She developed classical symptoms of polydipsia, polyuria - 2 weeks

Examination findings and Lab

- Clinically stable
- No dehydration
- No acidotic breathing
- Hemo dynamically stable
- Normal systemic examination.
- Random blood sugar - 540 mg/dl
- HBA1c - 9.1
- Urine ketones negative
- Serum bicarbonate - 23 meq/L
- Venous blood gas - pH 7.41

Initial management

- Started on plain insulin on a sliding scale
- Total daily requirement of insulin was assessed.
- Shifted to basal bolus insulin regimen:
 - a) Basal insulin - 1 nj Glargine (0.25 IU/kg)
 - b) Bolus insulin - 1 nj Aspart (1U for 15 grams of carbohydrate intake)

Diabetic Team – identified roles

Educator	Dietician	Physicians
Insulin administration	Carbohydrate counting	Insulin dose adjustment
SMBG and maintenance of diary	Calculation of bolus dose	Ketone testing and sick day management
Hypoglycemia recognition and therapy	Reading food labels	Importance of glycemic control

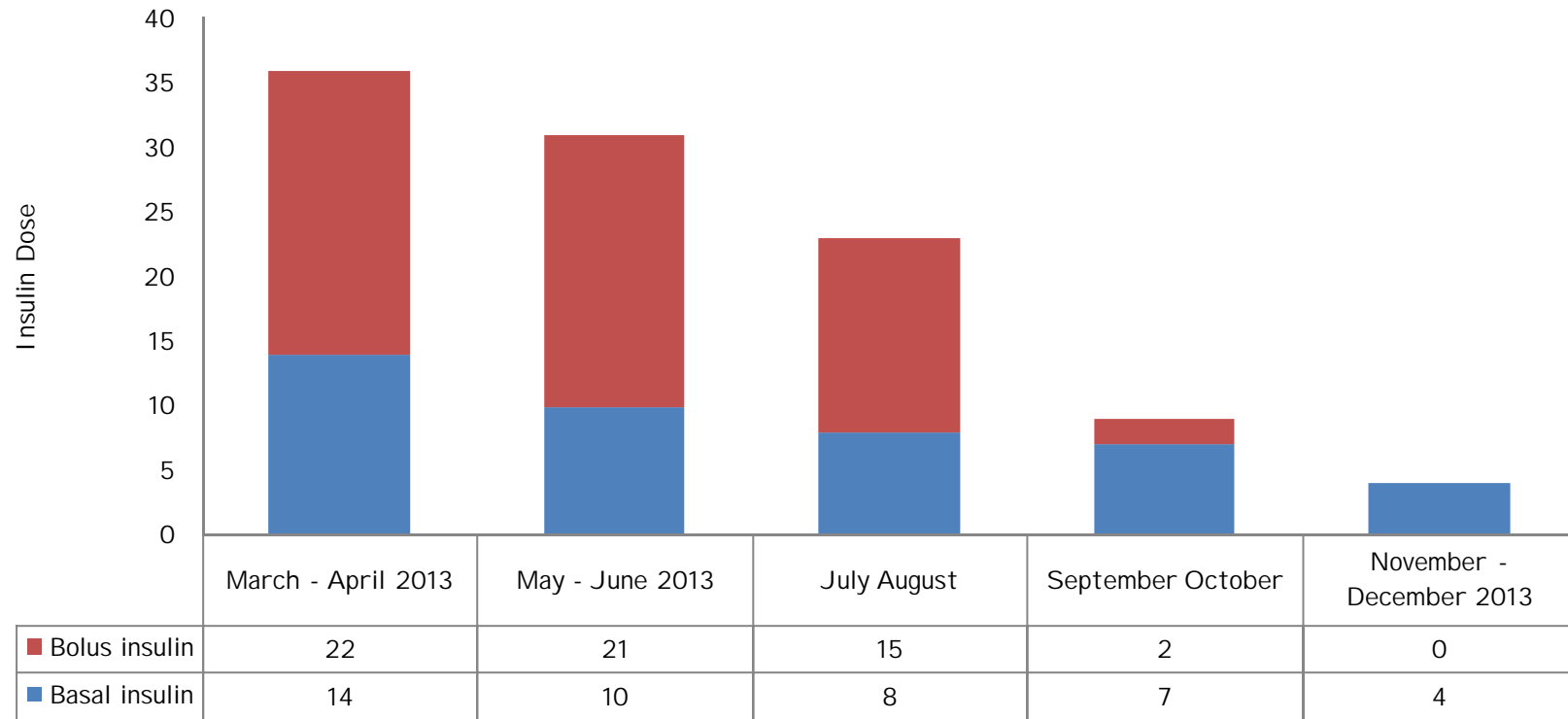
Further evaluation

- HBA1C – 9.1
- C-peptide – 4.6 ng/mL (Normal Range: 1.1-4.4 ng/ml)
- Anti GAD – antibody negative

Child was discharged (weight 20.1 kg) on
Glargine 14 IU/day

Aspart for meals (as per carbohydrate intake –
18-22 units/day)

Insulin requirement



Tac dose - 3 mg/day

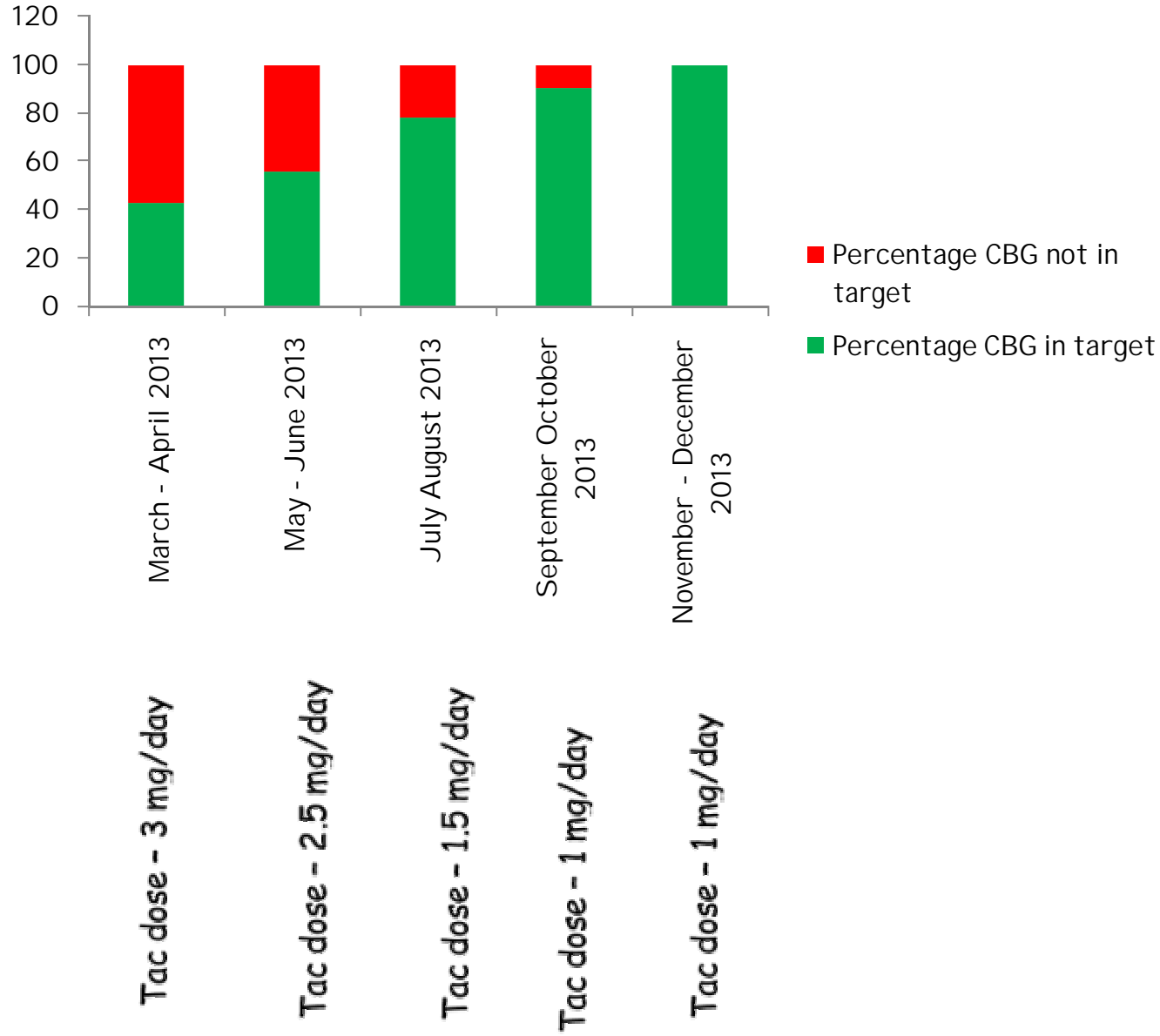
Tac dose - 2.5 mg/day

Tac dose - 1.5 mg/day

Tac dose - 1 mg/day

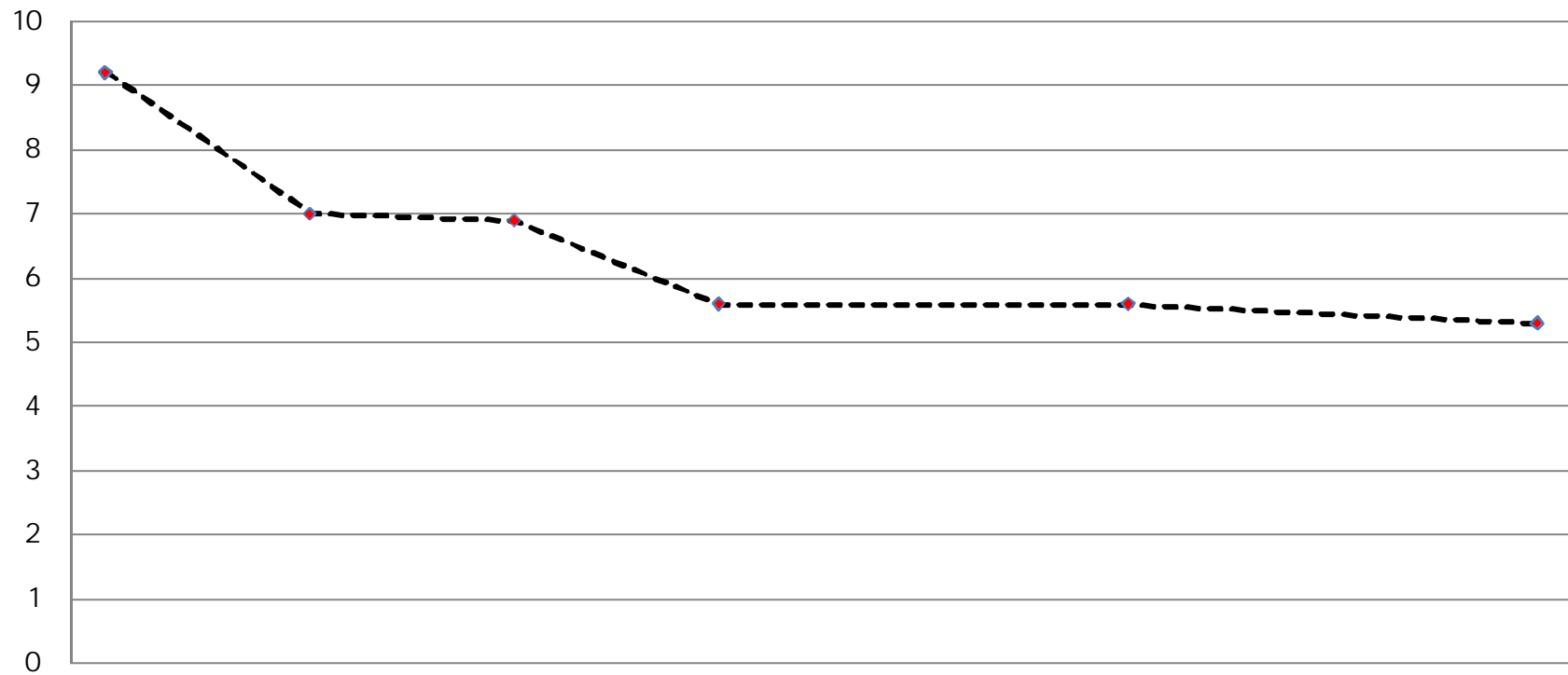
Tac dose - 1 mg/day

Glycemic control



HBA1C

HBA1C



	Mar-13	Jun-13	Sep-13	Dec-13	Jun-14	Dec-14
---◆--- HBA1C	9.2	7	6.9	5.6	5.6	5.3

- Tacrolimus levels checked twice in the recommended range(8.2 ng/ ml and 10.2ng/ml), hence tacrolimus tapered
- Insulin therapy was stopped in December 2013.
- On follow-up for the past 1 year
- No further hyperglycemia symptoms.
- Maintaining non-diabetic range HBA1C.
- Maintaining good renal functions.

Review of literature

- PTDM (Post Transplant Diabetes Mellitus)/
NODAT (New Onset Diabetes after
Transplantation) – Mechanisms:
 - a) Immunosuppressive therapy (Tacrolimus)
 - b) Concomitant Steroid therapy
 - c) Growth hormone therapy
 - d) Peripheral insulin resistance
 - e) Underlying disease

Why diabetes?

- Previously – insulin resistance
- Dose dependant reduction in phase 1 insulin secretion
- Reduced functional reserve of hormone production of beta cell
- REDUCED TRANSCRIPTION OF INSULIN GENE – CURRENT CONCEPT

Principles of therapy

- Starting dose – 0.05 mg/kg to 0.15 mg/kg BD.

Timing post transplant	Tacrolimus level
1 st 2 weeks	20-25 ng/ml
1 month	15-20 ng/ml
3 month	10-15 ng/ml
chronically	5 – 10 ng/ml

- Tacrolimus levels > 20 ng/ml – risk of DM
- Cyclosporine may be an alternative – cosmetic side effects in a girl child

Paediatric experience - Developed world

Author	Reference	Data	Risk factors
Dittrich et al	Ped Nephrol 2006	Series of 5 cases of SDNS - 2 DM	Tacrolimus levels, family history of DM
Prokai A et al	Ped transplant 2005	6 out of 45 (13%) developed DM	Tacrolimus levels, systolic BP and elevated triglycerides
Guidofiller et al	Nephrol dial transplant 1997	Case report	Tacrolimus levels
Ron Shapiro et al	Transplantation 1999	9%	Tacrolimus levels
Eba H et al	American J of transplantation 2003	1.8%	Tacro levels, Older age and HLA DR matching
Wagner K et al	J Heart Lung transplant 1997	12/28 (43%)	Tacrolimus levels, pulsed steroid therapy

Paediatric experience – Developing world

Author	Reference	Data
Massod et al	Journal of Pakistani Medical Association	Series of two cases (hepatic transplant and Lawrence Moon Biedl syndrome)
Sarkar et al (Kolkotta)	Indian J pediatrics 2013	Child with SRNS – developed reversible diabetes
Manisha Sahay et al (hyderabad)	SJKDT 2013	Adults undergone renal transplantation – 20% developed NODAT (cyclosporine)
Jai Prakash et al (BHU Varanasi)	Indian Journal of Transplantation	Adults undergone renal trasnplantation (not related to drugs)

In a nut shell...

- Any child developing diabetes in post transplant period – NODAT/ PTDM

Ascertain by History:

- a) Classical symptoms of DM
- b) Usage of Tacrolimus – are levels monitored?
- c) Pulse/ Low dose steroid therapy?
- d) Family history of type-2 diabetes.
- e) Severity of renal failure
- f) Usage of GH therapy
- g) Weight loss

On examination:

- a) Is the child dehydrated
- b) Is the child acidotic

Work-up

- a) WHO criteria for diabetes
- b) HBA1C
- c) C-peptide
- d) Anti GAD antibody
- e) Tacrolimus levels

Principles of therapy:

- a) Ascertain insulin requirement – start on Actrapid
- b) Shift to basal bolus insulin therapy.
- c) Monitor tacrolimus levels . Reduce tacro - Early insulin weaning (Bolus followed by Basal)

Other drugs related to drug induced secondary diabetes

- L-Asparaginase
- Pentamidine
- Nicotinic acid
- Glucocorticoids
- Thyroid hormone
- Diazoxide
- Beta adrenergic agonists
- Thiazides
- Dilantin

Take home messages...

- All children on calcineurin inhibitors need to be monitored for development of diabetes.
- Children who develop diabetes should be carefully followed-up to see if they outgrow the diabetes as the drug is tapered.
- It is easy to taper insulin on a basal bolus regimen.

Acknowledgement

- Chief Nephrologist and Consultant incharge - Dr Edwin Fernando
- Transplant Surgeon - Dr D Chandrasekar
- Pediatric Diabetes unit - Dr Thangavelu S, Dr Hemchand K P (Paediatric Endocrinologist), Miss Saranya S (Dietician) and Miss Sherlin (Educator)



**HEAD OF
DEPARTMENT &
PEDIATRICIAN**



INTENSIVIST



**DIABETIC
DIETICIAN**



**DIABETIC
EDUCATOR**



ENDOCRINOLOGIST

THANK YOU