

39 year old F with sickle cell
anemia presenting with pain crisis

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11/8/12

HPI

- Knee and back pain typical of usual crises
- Nausea and vomiting 2 days prior to admission
- Had previously been on Lantus 15U daily that had been started in 2011
- Did not use Lantus for 2 days
- Not checking blood sugars at home

PMH

Sickle cell anemia

PE/DVT

CVA x 2

Asthma

DM

PSH

Cholecystectomy

FH

SCT parents, daughter

SH

No tobacco, etoh

Lives with 18 yo daughter

MEDS

Albuterol, T#4, Dilaudid,
Lantus 15U qHS,
Lisinopril 2.5 mg,
Gabapentin 300mg qHS,
Folic acid, Paxil 20mg
qday, Coumadin,
Oramorph

Physical Exam

Vitals: 36.4, 107/66, 90, 16, BMI 21, 95%RA

Gen: somnolent, appears in pain

CV: flow murmur

Pulm: clear bilaterally

GI: active emesis, soft, no rebounding or
guaring

Neuro: unable to assess orientation

Skin: no rash

Initial Labs

120	82	39	1321
5.7	9	1.5	8.8
AG 29			3.1
			4.7

6.4	
18	339
21	
PMN 87%	

8.3	4.7
2.2	152
21	19

HbA1c 7.4 %

Lipase 220 (13-60)

Ketones 8.17 (RR <0.30)

VBG pH 7.03

UA: 1.025, Neg LE/Nit/bact,
3+ glu, 2+ ketones

- Anti-GAD Ab 45 (RR < 0.02)
- C-peptide 0.04, Glucose 214
- Fructosamine 403 $\mu\text{mol/L}$ (RR 200-285)

Fructosamine HbA1c chart

Fructosamine (μmol)	HbA1c %	HbA1c IFCC (mmol/mol)
200	5	31
258	6	42
288	6.5	48
317	7	53
346	7.5	58
375	8	64
435	9	75
494	10	86
552	11	97
611	12	108

$\text{HbA1c} = 0.017 \times \text{Fructosamine} + 1.61$.
In our patient, calculated HbA1c = 8.5

Clinical Questions

- Incidence of diabetes in SCD/SCT?
- Glucose metabolism/insulin secretion in SCD?
- Prevalence of diabetes-related autoantibodies in SCD?
- Assessing glycemic control in SCD/SCT?

Incidence of DM in SCD

- Concurrent sickle cell disease with diabetes is rare
- Type 1 Diabetes and sickle cell is even more rare
- Previous case reports were not associated with any diabetes complications

Reason for this uncommon association

- Previously patients with sickle cell anemia died younger so never manifested complications from diabetes
- Genetics?
 - No known association between inheritance patterns of diabetes and sickle cell hemoglobinopathies
 - Beta-globin and insulin genes are both on the short arm of chromosome 11

Prevalence of SCD + DM

- 185 total pregnant patients with hemoglobinopathy (123 SCT, 35 HbSS, 20 HbSC, 7 HbS-Thal)
- 2263 controls
 - 4% abnormal screening
- Screening at 28-30 weeks with 2h post-prandial glucose
- None of pregnant patients with sickle cell hemoglobinopathies demonstrated evidence of glucose intolerance

2h post-prandial plasma glucose

Hemoglobin	Early gestation (8–20 weeks)			Late gestation (28–32 weeks)		
	No. of patients	Range (mg/dl)	Mean (mg/dl)	No. of patients	Range (mg/dl)	Mean (mg/dl)
HbA-S	123	69–139	92.8 ± 12.2	64	60–128	90.1 ± 16.7
HbS-S	35	62–142	96.8 ± 10.6	35	68–136	92.5 ± 18.1
HbS-C	20	70–136	89.2 ± 15.2	20	64–168 ^a	93.5 ± 21.6
HbS-Thal	7	59–121	86.8 ± 16.8	7	56–132	88.6 ± 19.2
Control ^b	2263	64–197	104 ± 21.6	2263	68–322	107 ± 22.0

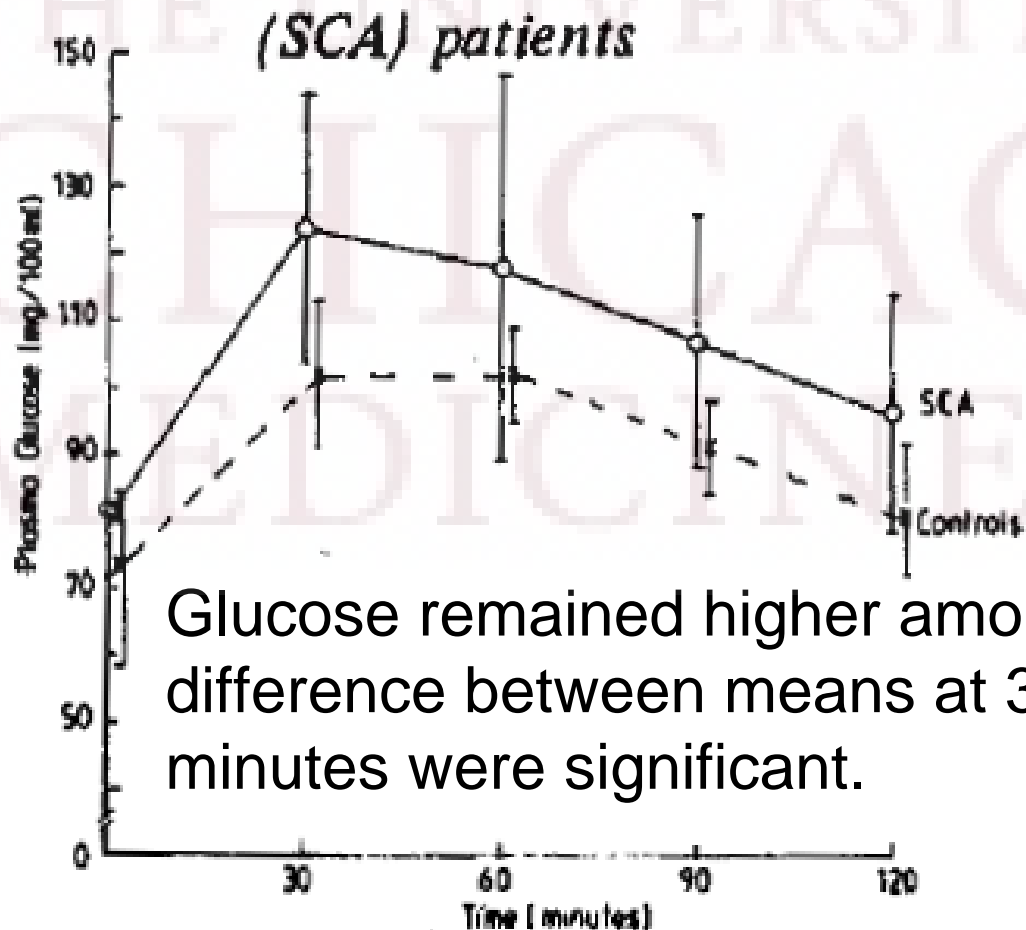
Controls: 14 had an abnormal early screening.
73 had an abnormal late screening.

Test group: no abnormal screenings early or late.

OGTT in SCD

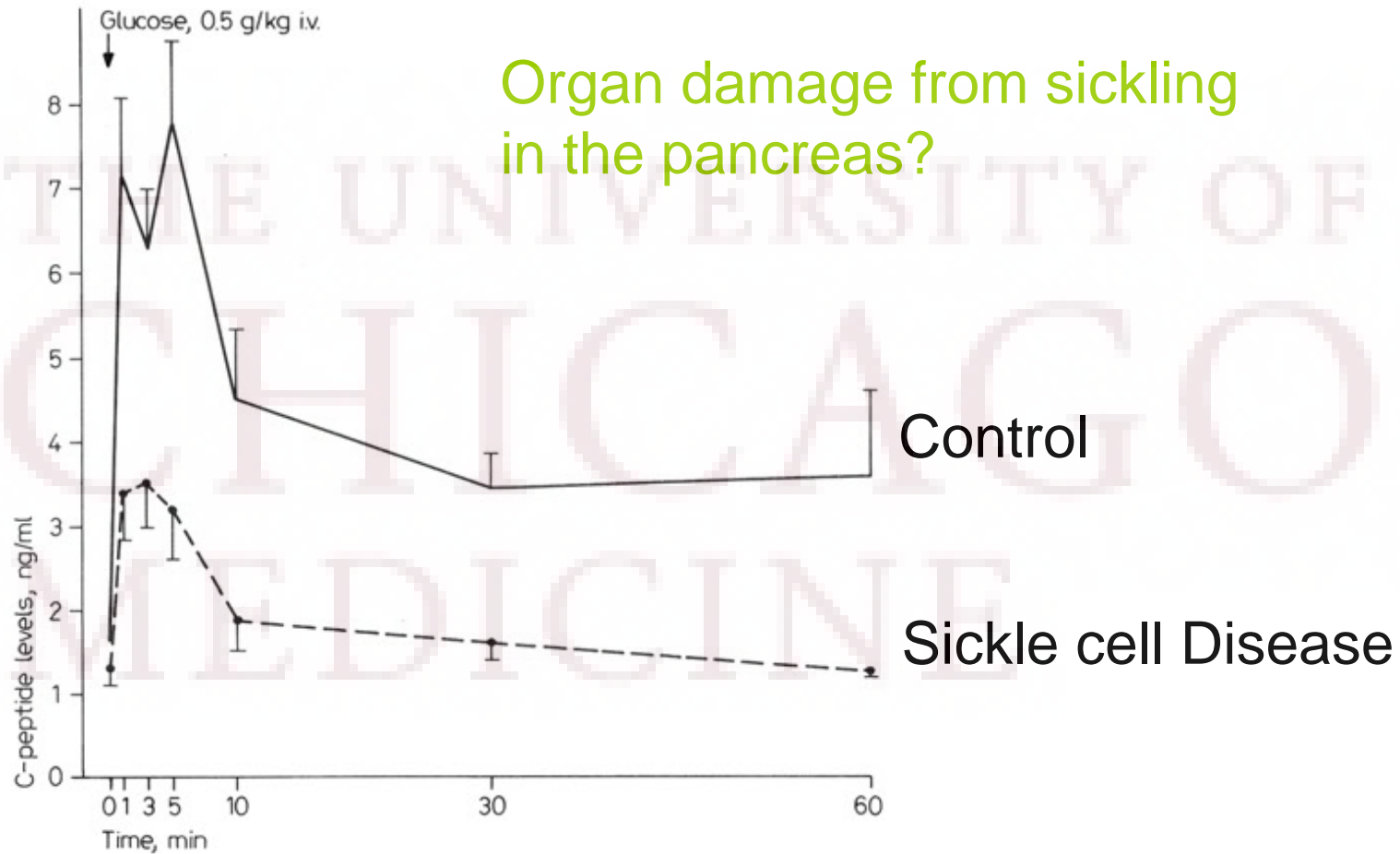
- 12 kids with SCD, 9 controls

Mean fasting glucose was higher in SCD than in controls (81 vs 72).



Glucose remained higher among SCD. The difference between means at 30, 90, 120 minutes were significant.

C-peptide secretion in SCD



Serum c-peptide levels at 0, 1, 3, 5, 10, 30, 60 minutes after glucose infusion

Sickle Cell Trait and DM

- These conditions co-exist in >1 million worldwide
- In the US in 2008 the prevalence of diabetes and HbC or HbS trait was about 350,000.
- No evidence that SCT affects course of DM

Diabetes-related autoantibody Prevalence

- Prospective screening for hyperglycemia in pediatric ED
 - 30 hyperglycemic patients
 - 30 stress control subjects
 - 30 healthy controls
- 3.8% (35 of 926) ED patients were hyperglycemic. Mean glucose 192 mg/dL.
- Tested for ICA, IAA, GAD, HLA typing
- Results: After 30-36 months of follow-up no patients or controls developed diabetes. 4 of 8 patients with SCD had insulin autoantibodies compared with 0 of 52 ED patients without SCD.

Assessing glycemic control in SCD

- RBC life span is about 10-14 days
- HbA1c does not accurately represent glycemic control
- Fructosamine- avg blood glucose over a period of 2-3 weeks
- Both SCD and DM are associated with renal impairment and retinopathy
- Ketoacidosis and the associated dehydration can precipitate sickle cell crisis

Fructosamine study

- 150 patients with sickle cell disease
- 100 controls- non-diabetic
- 50 type 2 diabetics
- Mean glucose/fructosamine
 - SCD: 4.3 mmol/L (77 mg/dL)– 1.3 mmol/L
 - Controls: 4.6 mmol/L (83 mg/dL)– 3.2 mmol/L
 - T2DM: 18.2 mmol/L (328 mg/dL)– 1.4 mmol/L

Table i: Serum fructosamine, fasting glucose ,albumin and total bilirubin (Mean \pm SEM and Range) in HbSS patients, Diabetics and Controls.

	HbSS Patients n = 150	Diabetics n = 50	Controls n = 100
Fructosamine (mmol/L)	1.3 \pm 0.16 (0.7-1.9)	3.2* \pm .16 (1.0-5.2)	1.4 \pm 0.04 (0.6 - 2.2)
Glucose mmol/L	4.3 \pm 0.07 (2.5-6.1)	18.2* \pm 0.01 (4.0-32.4)	4.6 \pm 0.07 (2.0–7.2)
Albumin g/L	40.0 \pm 0.47 (28-52)	38 \pm 0.58 (29 - 45)	38 \pm 0.38 (30 - 45)
Total Bilirubin μ mol/L	43* \pm 1.7 (0-85)	14 \pm 0.5 (0-17)	15 \pm 0.9 (0-17)

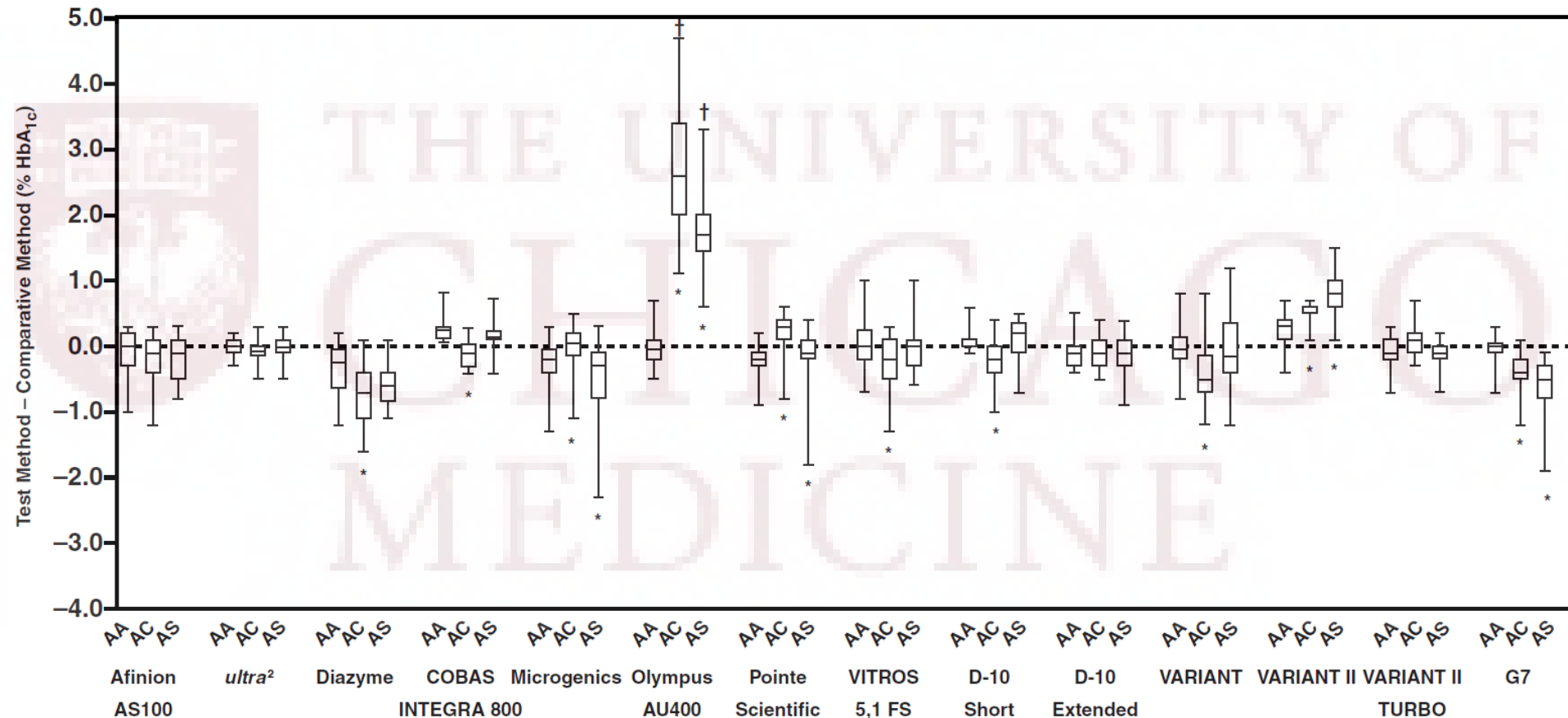
* Significant difference (P < 0.05)

Table ii: Serum fructosamine(Mean \pm SEM and Range) at different levels of serum total bilirubin concentrations in HbSS patients.

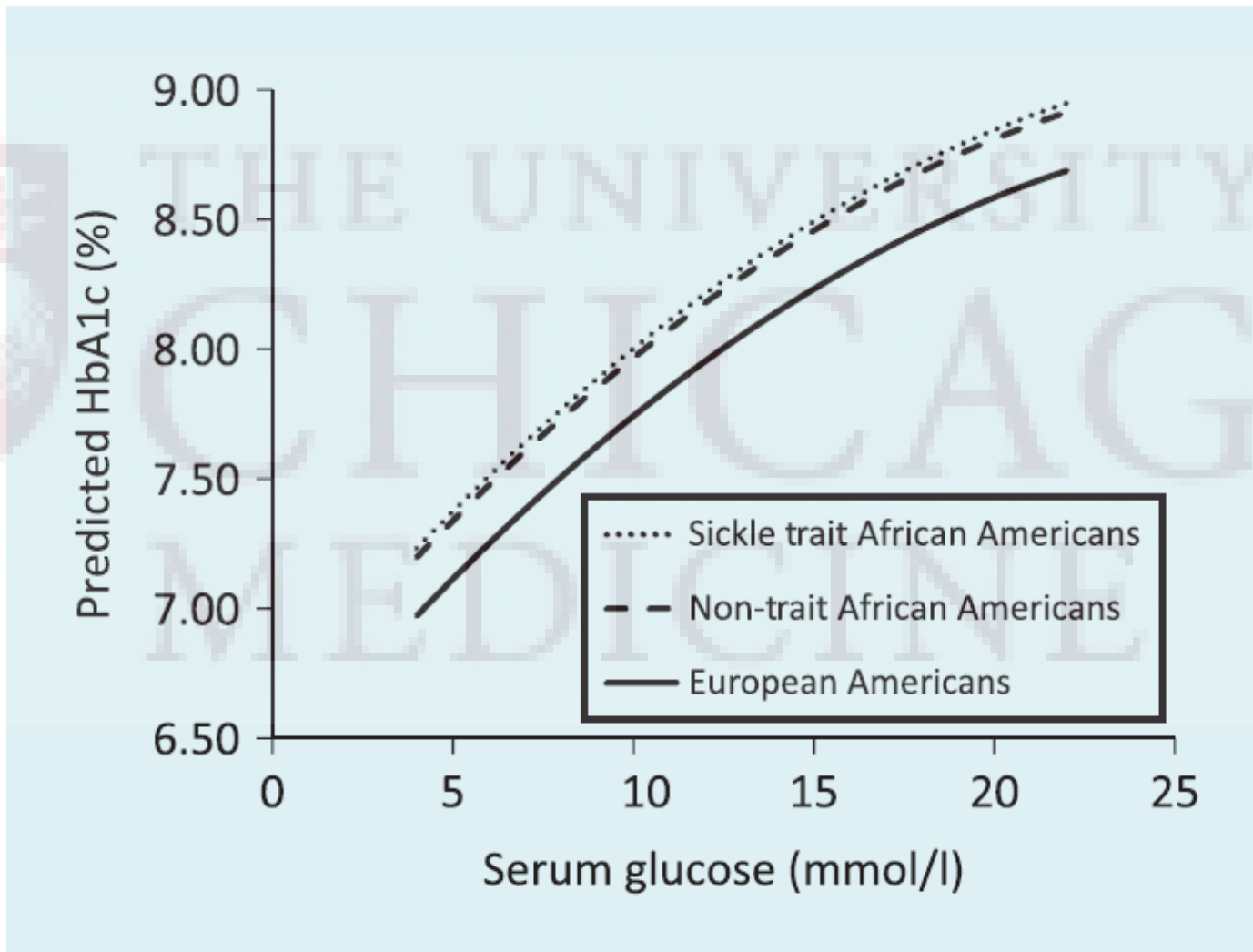
Bilirubin (μmol/L)	No of (HbSS) patients	Fructosamine (mmol/L)
11-80	83	1.3* \pm 0.11 (0.62 – 1.98)
81 – 160	67	1.4* \pm 0.12 (1.22 – 1.98)

* No significant difference (P >0.05)

Effect of SCT on HbA1c?



Effect of SCT on HbA1c?



Take home points

- Concurrent Sickle cell anemia and Diabetes is very rare
- Need more studies looking into insulin secretion, autoantibodies in SCD
- HbA1c is not reliable in sickle cell anemia but can be used in sickle cell trait
- Fructosamine is a better measure of glycemic control in sickle cell anemia

References

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