HYPOGONADISM, BONE MINERAL COMPOSITION AND LIPID ABNORMALITIES IN ADULT MALE PATIENTS WITH SICKLE CELL DISEASE

Sickle Cell Unit
UWI, Jamaica

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Background

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- Hypogonadism is defined as serum testosterone < 300 ng/ml (12 nmol/l) combined with at least one clinical symptom or sign of the disorder
- In adult males, the disorder may manifest with reduced libido, erectile dysfunction, cognitive delays, easy fatigability and difficulty in concentration, reduced muscle and bone mass.

Background

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- Hypogonadism has been recognized in adolescent and young adult males with sickle cell anemia.
- Possible causes of hypogonadism in sickle cell anemia include primary testicular failure or hypothalamic or pituitary dysfunction.

Background

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- Recent studies in other patient populations, have reported the association of reduced serum testosterone levels with obesity, the metabolic syndrome and Type 2 diabetes mellitus.
- Hypogonadism is also associated with anemia and increased visceral or abdominal adiposity and reduced bone mineral density.

Background

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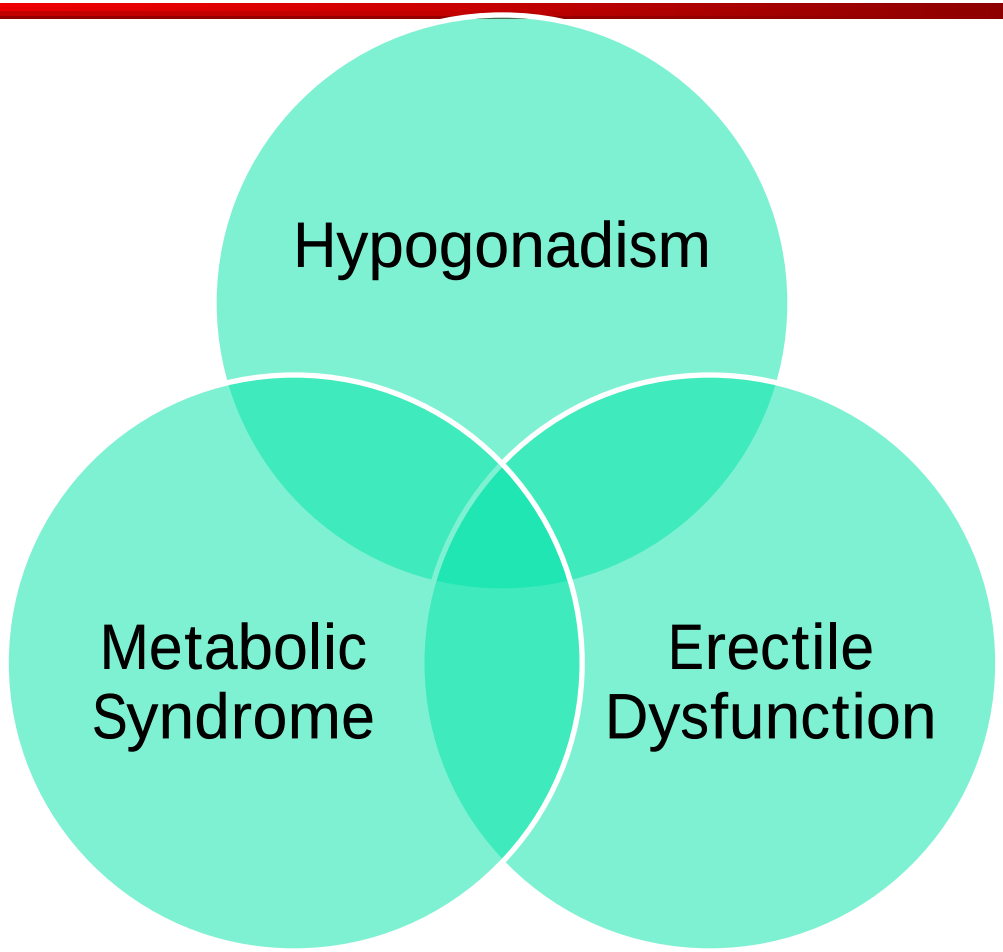

Background

- These adverse effects of hypogonadism, not only affect quality of life, but also increase morbidity and mortality.

Decline in Testosterone Levels is Associated with Co-Morbid Conditions rather than with Age

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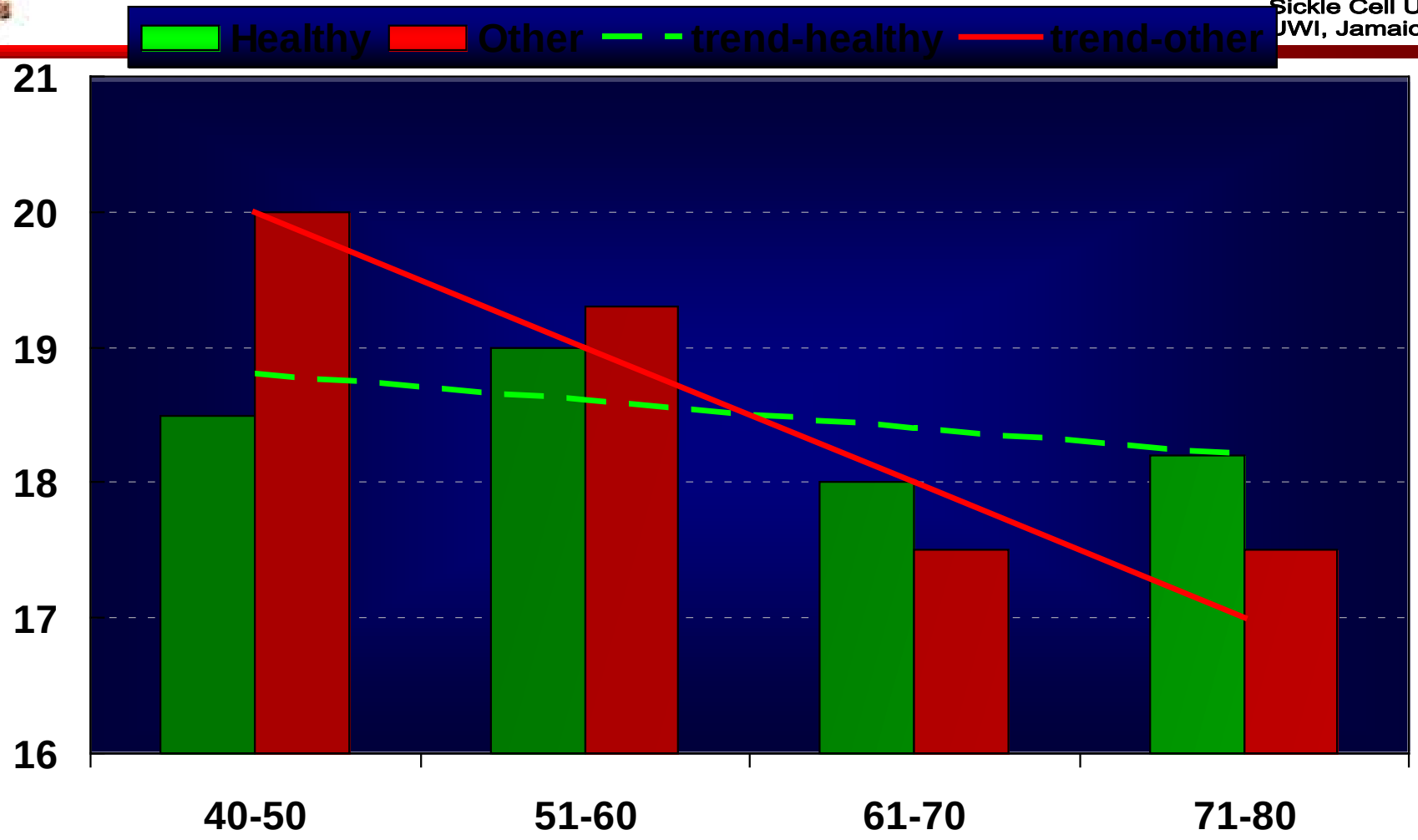

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Aim

- To determine differences in hypothalamus-pituitary-gonadal axis, and the effect of these differences on cholesterol, body and bone composition in adult males with sickle cell disease.

Design and Methods

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- Cross-sectional study
- Recruitment: July-October 2010
- Cases
  - Fifty (44) male patients with sickle cell anemia, attending the Sickle Cell Unit, University of the West Indies, Jamaica for health maintenance visits
  - All patients were in a clinically steady state
- Controls
  - Fifty (46) age-matched males with haemoglobin AA
- Patients were recruited in 3 age categories: 20-30 yrs; 31-40 yrs and 41-50 yrs

Design and Methods

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- Exclusion criteria: acute illnesses, endocrine disorders, and testosterone or bisphosphonate therapy.

Design and Methods

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- Blood taken, between 8:00 and 11:00 am
- Total and free testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, complete blood count (CBC) and lipid profile (serum triglycerides, HDL and LDL cholesterol)
- All controls had haemoglobin types determined by cellulose acetate electrophoresis to verify HbAA status
- All patients with sickle cell anemia had serum lactate dehydrogenase (LDH) measured as a disease severity index
- Weight (kg) and height (m) were measured and Body mass index (BMI) was calculated as weight (kg)/ height (m) ^{2}.

Design and Methods

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- Bone mineral density was measured with dual X-ray absorptiometry (DEXA)
  - *Lunar Prodigy Advance densitometer using encore 2007 program, Version 11.40.004*
    - Total body composition
    - Lean mass (kg)
    - Absolute whole body bone density
    - Total body bone mass

Design and Methods

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Table 2. WHO Diagnostic Categories of Bone Mineral Density.*

Diagnostic Category	Criterion
Normal bone mass	A value for bone mineral density or bone mineral content within 1.0 SD of the reference mean for young adults (T score –1.0 or higher)
Low bone mass (osteopenia)	A value for bone mineral density or bone mineral content that is more than 1.0 but less than 2.5 SD below the mean for young adults (T score between –1.0 and –2.5)
Osteoporosis	A value for bone mineral density or bone mineral content that is 2.5 SD or more below the mean for young adults (T score –2.5 or lower)
Severe osteoporosis (established osteoporosis)	A value for bone mineral density or bone mineral content that is 2.5 SD or more below the mean for young adults in combination with one or more fragility (low-trauma) fractures

* This information is from the World Health Organization (WHO) and was originally developed for white postmenopausal women but is now also applied to men.

Results

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Testosterone status in study patients

Testosterone Status	Patients with sickle cell disease (n ;%)	Controls (AA genotype) (n; %)
Eugondal	31 (71)	40 (87)
Hypogonadal	13 (29)	6(13)
	44(100)	46 (100)

Results

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Mean Serum Hormone Levels	Patients with sickle cell disease	Controls (AA genotype)	p Value
Mean ± s.d.Total Testosterone (nmol/L)	14.7 (13.2,16.3)	18.3 (16.4,20.5)	<0.005
Mean ± s.d.Free Testosterone (pmol/L)	27.3 (24.1,30.8)	30.3 (35.9,45.3)	<0.0001
FSH (IU/L)	7.5±4.9	4.4±2.4	<0.0003
LH (IU/L)	7.3±3.3	4.9±3	<0.0006
Prolactin (mIU/L)	224.3±178.5	149.3±63	<0.009

Results

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Variable	Patients with sickle disease	Controls (AA genotype)	p Value
Total Cholesterol (mM/L)	3.0±0.6	4.8±0.8	<0.0001
HDL Cholesterol (mM/L)	0.9±0.2	1.3±0.3	<0.0001
LDL Cholesterol (mM/L)	1.7±0.5	2.9±0.8	<0.0001
Triglycerides (mM/L)	1.2±0.5	1.4±0.9	0.3
Cholesterol/ HDL Cholesterol	3.6	3.9	0.2

Results

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Variable	Patients with sickle disease	Controls (AA genotype)	p Value
Haemoglobin (g/dl)	7.7±1.6	14.4±1.2	<0.0001
MCV (fL)	87.9±8.5	88.6±5.0	0.6
MCH (pg)	30.2±3.5	29.3±2.1	0.1
MCHC (g/dl)	34.3±1.1	32.8±1.8	<0.0001
WBC (10^9/L)	10.9±3.2	5.8±2	<0.0001
Plt (10^9/L)	376.9±143.2	251±61.6	<0.0001
LDH IU/L	1352.5±478.9	619.7± 145.1	<0.0001

Results

Variable (mean ± s.d.)	Patients with Sickle Cell Disease	Controls	p value
Height (cm)	175.5±7.1	174.6±6.9	0.5
Weight (kg)	62.1±9.1	79.9±13.5	<0.0001
BMI (kg/m^2)	20.2±2.7	26.2±4.3	<0.0001
Lean mass (kg)	50.3±5.9	58.5±6.4	<0.0001
Bone mass (kg)	2.8±0.6	3.4±0.4	<0.0001
Absolute whole body bone density	1.2±0.1	1.3±0.1	<0.0001
T score	-0.3±1.8	1.0±1.3	<0.0001
Z score	-0.7±1.7	-0.1±1.1	0.06

Testosterone Concentrations by Age-group

Values are mean ±sem

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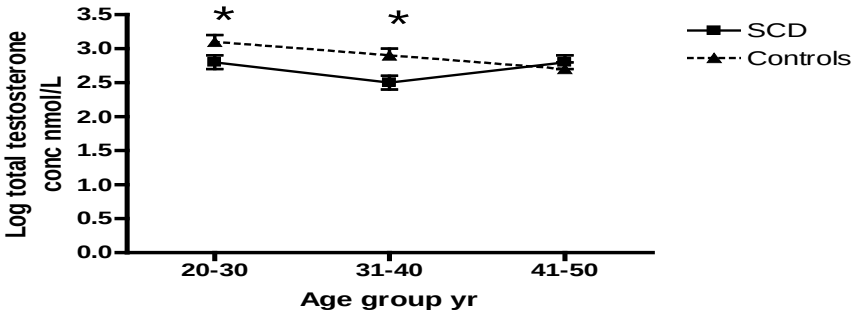

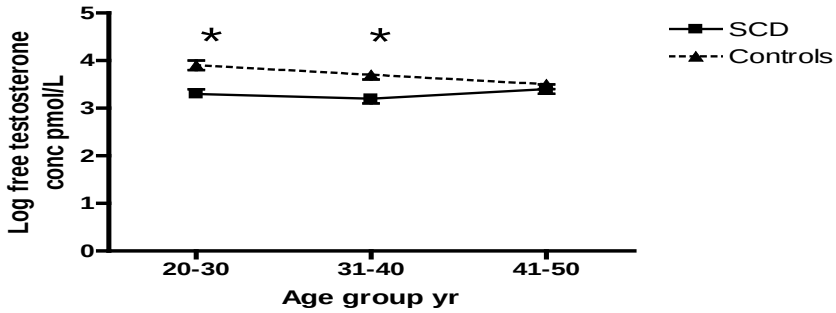

* $p<0.05$

Conclusion

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- Hypogonadism is common in sickle cell disease and is due to primary testicular failure.
- Adult males with sickle cell disease are more wasted with lower bone composition and lipid levels compared with AA controls

Summary

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- Hypogonadism is a problem in adult males with sickle cell disease.
- The association of this abnormality with metabolic abnormalities and bone density changes may require further studies.
- We are currently conducting a trial using Nebido® in male patients with sickle cell disease and hypogonadism.