The endocrine and metabolic characteristics of a large Bardet-Biedl syndrome clinic population

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Introduction

Bardet Biedl syndrome (BBS) is a rare autosomal recessive disorder caused by ciliary dysfunction. It is characterised by rod cone dystrophy, polydactyly, renal dysfunction and cognitive impairment.

Endocrine consequences include obesity and hypogonadism in males. It is reported that 72%-96% of postpubertal BBS patients are overweight (1,2). The prevalence of type 2 diabetes has been found to be 48% in 1 cohort and hypertension is also thought to be prevalent (1). The prevalence of metabolic syndrome in BBS is unknown although higher levels of triglycerides, central obesity and diastolic blood pressure have been found in children with BBS compared to age and BMI matched controls (3).

The prevalence of hypogonadism in BBS males has been reported to be as high as 97% (2). However, this was based on structural abnormalities rather than biochemical evidence.

A previous study has reported high levels of pituitary abnormalities in a paediatric BBS population (4).

We aimed to identify the prevalence of type 2 diabetes. metabolic syndrome and hypogonadism in a large adult BBS cohort. We assessed pituitary and thyroid function in patients with BBS.

Methods

One hundred and fifty-four patients with BBS were identified through 2 national BBS clinics. Anthropometric measurements and fasting blood samples were taken in one hundred and thirty patients. Metabolic syndrome was defined using the International Diabetes Federation criteria (5).

Data are reported as mean ± standard error of the mean (SEM).

Results

Male: Female	85:69 (55.2%:44.8%)
Age	33.0 ± 1.0 yrs
BMI	35.7 ± 0.7
Height (cm)	101.3 ± 24.8 (133)
Weight (kg)	167.8 ± 10.8 (125)
Ethnic Origin: -White Caucasian -Middle Eastern -South Asian	 128 (83.1%) 13 (8.4%) 13 (8.4%)

Table 1: BBS patient demographics

Results

Biochemical parameter	BBS subjects (n) Mean ± SD
Fasting glucose (mmol/L)	5.2 ±1.2 (109)
Fasting insulin (pmol/L)	24.2±17.0 (46)
HbA1c (%)	6.0±1.4 (101)
Cholesterol (mmol/L)	4.9±1.0 (129)
HDL Cholesterol (mmol/L)	1.2±0.3 (126)
LDL Cholesterol (mmol/L)	2.8±0.9 (84)
Triglycerides (mmol/L)	2.0±1.2 (130)
Systolic BP (mmHg)	135.2±18.3 (100)
Diastolic BP (mmHg)	81.4±11.4 (100)
Raised alanine transaminase (ALT)	26.8% (34/127)

Table 2: Metabolic characteristics of patients with BBS

The prevalence of metabolic syndrome was high (59.4%).

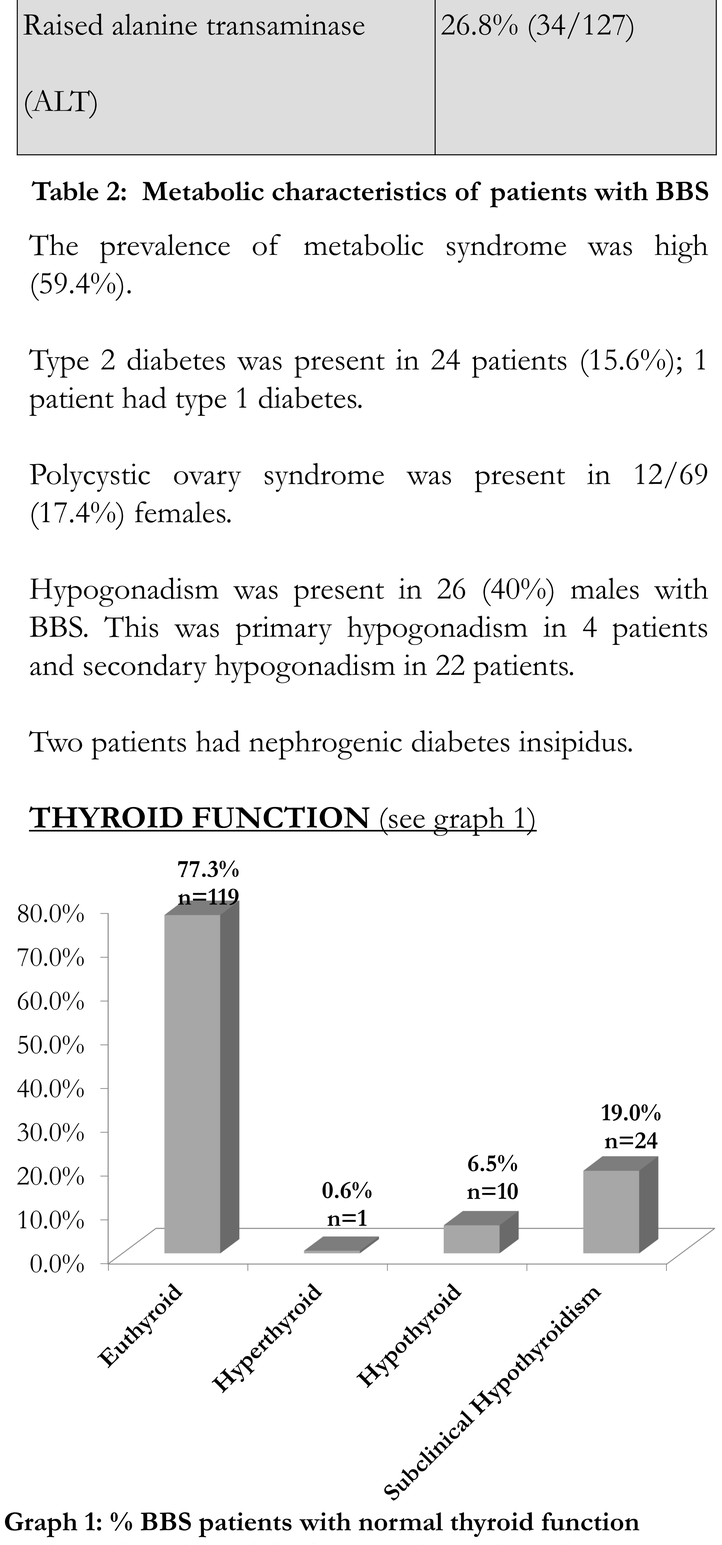
Type 2 diabetes was present in 24 patients (15.6%); 1 patient had type 1 diabetes.

Polycystic ovary syndrome was present in 12/69 (17.4%) females.

Hypogonadism was present in 26 (40%) males with BBS. This was primary hypogonadism in 4 patients and secondary hypogonadism in 22 patients.

Two patients had nephrogenic diabetes insipidus.

THYROID FUNCTION (see graph 1)



Graph 1: % BBS patients with normal thyroid function (euthyroid) or thyroid dysfunction (hyperthyroidsm hypothyroidism or subclinical hypothyroidism).

PITUITARY FUNCTION (Table 3)

Eupituitary	**102 (78.4%)**
Abnormal pituitary function: -Isolated low IGF-1 -Isolated low prolactin -Mild Hyperprolactinemia (Prolactin <1000mIU/l) - Severe Hyperprolactinemia (Prolactin>6000IU/l)	**28 (21.5%)** 15 (11.5%) 7 (5.4%) 5 (3.8%) 1 (0.8%)

Table 3: Table showing abnormal pituitary function in the BBS cohort

RENAL STATUS

Four (3.4%) patients had stage 5 CKD, 4 (3.4%) stage 4 CKD and 14 (11.8%) stage 3 CKD. Four patients had functioning renal transplants.

Conclusions

This is the first study to investigate endocrinopathies in a large BBS population. Despite previous reports, generalised pituitary hormone dysfunction is not prevalent however subclinical hypothyroidism in our cohort and hypogonadism in males is common. The majority of patients are obese and the prevalence of metabolic syndrome is high despite a mean age of 33 years in this cohort. Those with metabolic syndrome are at an increased risk of developing cardiovascular disease and type 2 diabetes at a later stage and therefore timely intervention for reversible risk factors such as obesity is important.

References

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