Prevalence of Bardet–Biedl syndrome in Tunisia

Oussama M'hamdi · Ines Ouertani · Faouzi Maazoul ·
Habiba Chaabouni-Bouhamed

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Abstract Bardet–Biedl syndrome (BBS, OMIM 209900) is a ciliopathy causing multivisceral abnormalities. This disease is mainly characterized by obesity, post-axial polydactyly, hypogenitalism, intellectual disabilities, pigmentary retinopathy, and renal deficiency. The prevalence of BBS has been estimated in different populations, ranging from 1 in 160,000 in European populations to 1 in 13,000 in Bedouins from Kuwait. In the present report, we present the first epidemiological study of Bardet–Biedl syndrome in Tunisia. From 1984 to 2009, 46 Tunisian families, including 67 affected members, were diagnosed as BBS. The patients' ages ranged between 6 months and 37 years, with median age of 10.4 years. High level of consanguinity was noted in our cohort (93.47%). The overall minimum prevalence in our population was estimated to be approximately 1 in 156,000 individuals. Our study reflects the actual frequency of BBS in North Africa and showed that this disease seems uncommon.

cardinal features: obesity, post-axial polydactyly, hypogonadism, intellectual disabilities, pigmentary retinopathy, and renal deficiency (Moore et al. 2005). BBS is a genetically heterogeneous disorder, and up to now, 14 genes have been described (*BBS1* to *BBS14*, namely *BBS1*, *BBS2*, *ARL6*, *BBS4*, *BBS5*, *MKKS*, *BBS7*, *TTC8*, *BBS9*, *BBS10*, *TRIM32*, *BBS12*, *MKS1*, *CEP290*). Mutations in *BBS1–14* account for over 75% of affected families (Zaghloul and Katsanis. 2009). The prevalence of BBS in Europe ranges from 1/125,000 to 1/160,000 (Klein and Amman 1969; Beales et al. 1997). In some isolated populations over the world, it was estimated to be 1 in 13,000 in Bedouins of Kuwait (Farag and Teebi 1989) and 1 in 18,000 in Newfoundland (Moore et al. 2005). However, the epidemiological criteria of this disease have not been studied in North Africa. In this study, we report briefly the first epidemiological study of BBS in North Africa.

To the editor,
Bardet–Biedl syndrome (BBS, OMIM 209900; Rooryck and Lacombe 2008) is a ciliopathy causing multivisceral abnormalities. This disease is defined by a combination of

Patients' features

From 1984 to 2009, 46 Tunisian families, including 67 affected members, were diagnosed with BBS. The patients were referred to the genetic department at Charles Nicolle Hospital in Tunis, which is the first center for diagnosis and/or genetic counseling in the country. The number of patients in the present study may not represent the real number of cases in Tunisia, but it can give an overview of the disease epidemiology in our population.

Clinical analysis revealed that of the 67 cases, 34 were males and 33 were females, and the male-to-female ratio

O. M'hamdi · I. Ouertani · H. Chaabouni-Bouhamed (✉)
Faculté de Médecine de Tunis, University Tunis el Manar,
Tunis, Tunisia
e-mail: habiba.chaabouni@rns.tn

F. Maazoul
Department of Hereditary Disorders, Charles Nicolle hospital,
Tunis, Tunisia

Table 1 Summary of clinical features for 67 BBS patients

Major criteria	Prevalence
Obesity	62/67 (92.53%)
Retinitis pigmentosa	58/67 (86.56%)
Post axial polydactyly	53/67 (79.10%)
Hypogonadism (males)	31/34 (86.20%)
Mental retardation and learning disabilities	35/67 (52.23%)
Renal abnormalities	13/67 (19.40%)
Other medical problems	
Neurological abnormalities	27/67 (40.29%)
Cardiopathy	7/67 (10.44%)
Deafness	8/67 (11.94%)

was 1.02. The patients' ages ranged between 6 months and 37 years, with median age of 10.4 years. Consanguinity was observed in 43 of the 46 families (93.47%). Patients were from North Tunisia (34 families, 73.91%), center (two families, 4.34%), and South Tunisia (ten families, 21.73%).

Obesity was present in 62 of 67 cases (92.53%, 95% confidence interval CI=89.98–93.33%). Retinitis pigmentosa was confirmed in 58 of 67 cases (86.56%, 95% CI=83.32–86.67%); other ocular abnormalities included strabismus, color blindness, astigmatism, macular edema, and nystagmus. Post-axial polydactyly was noted in 53 of 67 cases (79.1%, 95% CI=78.32–81.67%). Hypogonadism was present in 31 of 34 males (86.2%, 95% CI=84.52–87.87%), with micropenis or hypoplastic scrotum and cryptorchidism noted in six cases. Mental retardation and learning disabilities were present in 35 of 67 cases (52.23%, 95% CI=48.32–51.67%). Renal abnormalities was confirmed in 13 of 67 patients (19.4%, 95% CI=19.98–23.33%), including renal insufficiency and renal polykystosis in two cases (Table 1). Otherwise, different clinical features including neurological abnormalities were noted in 27 of 67 cases, including developmental delay (17/27) and behavioral trouble (8/27). Cardiopathy was present in 7 of 67 cases, and deafness in 8 of 67 cases was ascertained.

Discussion

BBS is a clinically and genetically heterogeneous disorder. The phenotype of BBS is highly variable. Clinical investigation during early infancy remains difficult, and some manifestations may occur during

childhood. The genetic heterogeneity of this disease with 14 defect genes described until now presents difficulties for the molecular testing of BBS. The recent development of BBS-ALMS array, which detects known mutations in these 14 genes, may play an important role in genetic evaluation strategies and counseling (Pereiro et al. 2011). Since the first report of BBS in 1920, this disease has been described in different populations. In the present report, we present the first epidemiological study of BBS from North Africa. The diagnosis of BBS in our cohort was based on the six cardinal criteria (obesity, retinal dystrophy, hypogenitalism and/or hypogonadism, post-axial polydactyly, learning disabilities, and renal abnormalities). The phenotype spectrum in our cohort was broader than the “classic package” since renal abnormalities have been added as new cardinal criteria for the diagnosis of BBS (Beales et al. 1999). As previously reported, variability was noticed in our BBS cohort families. Consanguinity rate was high in our group (93.47%) compared to other studies (Beales et al. 1999; Farag and Teebi 1988). The consanguinity rate was dramatically higher than reported in the Tunisian population (31.2%; Riou et al. 1989), which confirms the hypothesis that BBS is a rare disease in the region.

The overall minimum prevalence of BBS in Tunisia was found to be approximately 1 in 156,000. This frequency increases in the north, 1 in 87,000, which is about two times higher than the figure from the overall country. It may be explained by a clinical undervaluation of BBS in other health structures in the country. Usually, patients with complex dysmorphic syndromes, such as BBS patients, are referred to the genetic department at Charles Nicolle Hospital in Tunis, which is the main center for the diagnosis of congenital and hereditary disorders in Tunisia during 1984–2009. The current prevalence in our general population was low compared to that of 1 in 65,000 estimated in the Arab population of Kuwait (Farag and Teebi 1988) and 1 in 18,000 in Newfoundland (Moore et al. 2005); it borders the estimated prevalence in Europe (Rooryck and Lacombe 2008). In spite of limited study, our report should reflect the actual frequency of BBS in North Africa where the disease seems uncommon.

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