

BIO-DEMOGRAPHIC CHARACTERISTICS OF HOUSEHOLDS AND RISK FACTORS FOR DOWN SYNDROME IN MOROCCO

Zahra Oulmane¹, Mohamed Cherkaoui², Rekia Belahsen³, Mohamed Kamal Hilali²

¹Laboratory of Anthropogenetics, Biotechnologies and Health, Department of Biology, Faculty of Sciences, Chouaib Doukkali University, El Jadida 24-000, Morocco

²Department of Biology, Laboratory of Pharmacology, Neurobiology, Anthropobiology and Environment, Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco

³Laboratory of Biotechnology, Biochemistry and Nutrition, Training and Research Unit on Nutrition and Food Sciences, Department of Biology, Faculty of Sciences, Chouaib Doukkali University, El Jadida 24-000, Morocco

ABSTRACT

Background. The most studied risk factors for Down Syndrome (DS) were: region of residence, exposure to chemicals, parents' education level, cigarette and alcohol use by father or mother or both, and oral contraceptive (OC) use.

Objective. The aim of this study was to compare certain variables considered as risk factors on DS such as parental age at birth, OC use, child's sex, and rank of birth between children with DS and their siblings without DS as well as to determine the socio-bio-demographic characteristics of the families studied compared with the general Moroccan population.

Material and Methods. We conducted a cross-sectional analysis of 277 families with 925 siblings and at least one child with DS (279 with DS) between 2014 and 2017. The data are collected using a standardized questionnaire in Marrakech-Safi region. Data were entered and analyzed using the statistical program SPSS statistics software for Windows (version 20.0). Chi-square (χ^2) and Student t tests were used for testing statistical significance. Differences were considered significant when the p-value <0.05.

Results. The binary logistic regression analysis between DS and non-DS children in their bio-demographic characteristics studied (sex, maternal age at birth, paternal age at birth, oral contraceptive (OC) use, length of oral contraceptive use before pregnancy and rank of birth) showed that only maternal age and paternal age at birth and OC use were associated with DS birth (OR= 1.16; 95% CL: 1.11-1.21, OR= 1.05; 95%CL: 1.01-1.09 and OR= 0.01; 95%CL: 0.00-0.003, respectively). In the other hand, the comparison between socio and bio-demographic characteristics of households studied with data from National Population Survey and Family health (2018) showed a higher level of education in women and men in our sample. Similar results were shown in rate of men and women in paid employment, the rate of smoking and alcohol consumption among men and the rate of OC use before pregnancy among women.

Conclusion. These results will help to sensitize the Moroccan population about risk factors for DS.

Key words: Down syndrome, socio-bio-demographic factors, oral contraceptive, maternal age, paternal age, children, Morocco

INTRODUCTION

Down syndrome (DS) was discovered by *John Langdon Down* in 1866 [1], who described individuals with a common phenotype that called by his name.

Subsequently, the development of cytogenetic karyotyping has shown that DS is caused by the presence of extra chromosome 21 [2, 3], because of a meiotic nondisjunction error in the segregation of chromosome 21 during ovogenesis or spermatogenesis.

This extra chromosome 21 most often originates from the mother in approximately 95% of the cases of free trisomy 21 [4]. The most common type is associated with advanced maternal age, especially from approximately 35 years of age and above [5].

In addition to these genetic associations, several epidemiologic studies have shown a significant association between DS birth and environmental risk factors [6, 7, 8]. The most studied risk factors were region of residence, exposure to chemicals, parents'

Corresponding author: Zahra Oulmane, Laboratory of Biotechnology, Biochemistry and Nutrition, Training and Research Unit on Nutrition and Food Sciences, Department of Biology, Faculty of Sciences, Chouaib Doukkali University, El Jadida 24-000, Morocco, e-mail: z.oulmane@gmail.com

This article is available in Open Access model and licensed under a Creative Commons Attribution-Non Commercial 3.0.Poland License (CC BY-NC) (<http://creativecommons.org/licenses/by-nc/3.0/pl/deed.en>)

Publisher: National Institute of Public Health NIH - National Research Institute

education level, cigarette and alcohol use by father or mother or both, and oral contraceptive use. Within this list of risk factors, oral contraceptive (OC) use was of particular interest, as it is a more common habit than the others. The association of DS birth with this factor has been confirmed in several studies [7, 9] but contradicted in others [10, 11, 12].

The objectives of this study is to compare certain variables considered as risk factors on DS such as parental age at birth, OC use, child's sex, and rank of birth between children with DS and their siblings without DS as well as to determine the socio-bio-demographic characteristics of the families studied compared with the general Moroccan population.

MATERIAL AND METHODS

Subjects

Between May 2014 and November 2017, 277 families with DS child were enrolled in 11 associations and health centers that provided care and support for individuals with DS in; Marrakech, Safi, Chichaoua, El Kelâa of Sraghna, and Al Haouz in the Wilaya of Marrakech. Regarding the centers chosen, we placed a request attached to the questionnaire to allow our interview with parents and explain the objectives of the study to the responsible of all centers and associations providing help to people with DS in Marrakech Safi region. The eleven centers in which the study was conducted came to those who accepted our request. Families with at least one child clinically and/or cytogenetically confirmed DS were included.

For this study, pregnancies resulting in live births without perinatal mortality, including deaths in the first week of life and fetal deaths (stillbirths) [13], were included. Our cases were children with DS (N=279), all the cases in this study were sporadic, except for two couples who had two children with DS. Siblings without DS were used as controls (N=646).

Procedures

Data were collected using a descriptive, retrospective, and analytical cross-sectional survey. The material support of our survey consists of a standardized questionnaire providing information about the identity, socio-economic, bio-demographic, and cultural conditions of parents. The socio-bio-demographic variables used in this study were mean size of households, woman's level of education, man's level of education, mean paternal age at first marriage, mean age difference between spouses, kinship, synthetic fertility index SFI, mean number of live births, contraceptive use before pregnancy, cigarette smoking and alcohol consumption.

The independent variables used in this study were parents' age at birth, length of OC use before pregnancy,

sex of birth and rank of birth. The dependent variable was adjusted for children with DS.

Our study was designed in accordance with the Declaration of Helsinki. It was conducted in full respect of local ethical considerations, namely obtaining prior authorization from the competent authorities of the University and the responsible of the visited centers. We contacted the parents/guardians of people with DS to whom we presented the objectives of the investigation and enlightened them on their rights. The principle of volunteering for participation as well as the confidentiality and anonymity of the questionnaire were respected. A written parental consent form was received before the study.

Statistical analysis

Statistical analysis was done using the statistical program SPSS software for Windows (version 20.0). A descriptive analysis was performed using means, standard deviations (SD), and proportions as appropriate. To estimate the significance of the differences observed between the means, the student t test for normally distributed data was used. *Chi-square* (χ^2) test was used for categorical variables and differences were considered significant when the p-value was <0.05 . The binary logistic regression analysis which allows the elimination of confounding factors and entering the weight of the associated variables with DS birth in the bivariate analysis ($P<0.2$), was used to identify factors independently associated with DS birth. Associations were measured in odds ratio (OR) with 95% confidence intervals (95% CL).

RESULTS

Comparison of bio-demographic characteristics between DS and non-DS children studied

Table 1 gives the results of bivariate comparison of sex, maternal age at birth, paternal age at birth, oral contraceptive use, length of oral contraceptive use before pregnancy, and rank of the birth between DS and non-DS children studied. Except for the sex of the children, who is not statistically significant between groups (children with DS and their siblings without), all others variables studied, are strongly associated with DS. The mean maternal and paternal age at birth with DS was higher than that of non-DS birth, with a very significant statistical difference (35.95 ± 6.45 years vs. 28.49 ± 6.47 years and 42.20 ± 7.94 years vs. 35.56 ± 7.13 years, $p<0.0001$, respectively). The rate of OC use before DS pregnancy was higher than that of non-DS one (60.9% vs. 45.2% , $p<0.0001$). The mean length of OC use before DS pregnancy was longer than that of non-DS pregnancy (3.39 ± 2.48 vs. 2.15 ± 1.74 years, $p<0.0001$). Regarding the rank of birth, we

Table 1. Distribution of the nature of birth according to oral contraceptive (OC) use and bio-demographic characteristics of the families surveyed

Variables	Modalities	DS birth	Non-DS birth	Test
Child sex	Male	(160 /279) 57.3%	(363/646) 56.2%	$\chi^2=0.10$ ns
	Female	(119/279) 42.7%	(283/646) 43.8%	
OC use before pregnancy	Yes	(167/274) 60.9%	(284/629) 45.2%	$\chi^2=19.05$ ***
	No	(107/274) 39.1%	(345/629) 54.8%	
Length of OC use (years), (Mean \pm SD)		3.39 \pm 2.48	2.15 \pm 1.74	t =5.64***
Maternal age at birth (years) (Mean \pm SD)		35.95 \pm 6.45	28.49 \pm 6.47	t =16.10***
Paternal age at birth (years) (Mean \pm SD)		42.20 \pm 7.94	35.56 \pm 7.13	t =11.79***
Rank of birth (Mean \pm SD)		3.07 \pm 1.88	2.51 \pm 1.74	t =4.38***

SD - standard deviation; χ^2 - *Chi*² test ; t - *Student* test; ns - not significant; ***: P< 0.0001

Table 2: Result of Binary Logistic Regression Model. Analysis between Down and non-Down syndrome variable and bio-demographic variables studied

Variables	Adjusted OR	(CL 95%)	p
Sex	1.04	(0.66-1.66)	0.84
Oral contraceptive use	0.001	(0.00-0.003)	<0.0001
Length of oral contraceptive use before pregnancy (years)	1.11	(0.99-1.25)	0.06
Maternal age at birth	1.16	(1.11-1.22)	<0.0001
Paternal age at birth	1.05	(1.00-1.09)	0.01
Rank of birth	0.86	(0.73-1.00)	0.06

OR = odds ratio; p= significance; CL= confidence limits, underlined= significant at 5%

found that children with DS are born in advanced ranks compared to non-DS children (3.07 \pm 1.88 vs. 2.51 \pm 1.74, p<0.0001).

To eliminate the confounding factors we applied the logistic regression method (Table 2). Through this analysis, maternal age at birth, paternal age at birth and OC use before pregnancy were the only variables that determine independently the recourse to birth with DS (OR= 1.16; 95%CL: 1.11-1.21, OR= 1.04; 95%CL: 1.00-1.09 and OR= 0.00; 95%CL: 0.00-0.003, respectively).

Socio-biodemographic characteristics of households

Table 3 gives the number and the percentage of modalities of qualitative variables and mean \pm standard deviation for quantitative variables of DS households studied and their comparison with data from national Moroccan population surveys [14, 15].

The results showed that the rate of women and men who have a higher level of education is higher than what was recorded at the ENPSF in 2018 [14] at national level and in Marrakech-Safi region (16.3%, 20.9%; 8.8%, 10.1% and 7.0%, 7.9%, respectively). The rate of men and women with paid employment in our sample is higher than the rate recorded nationally and regionally (82.7%, 21.4%; 62.0%, 13.1% and 63.0%, 9.3%, respectively). The rate of smoking among

men in our study is higher than the rate recorded nationally and regionally (50.8%, 21.9% and 22.4%, respectively). With regard to alcohol consumption, the consumption rate among our sample was higher than that recorded among young Moroccans according to the 2011 National Youth Survey [15] (29.0% against 15.0%). The couples who are kinship in our study represent 11.6%, this rate is lower than that recorded at the national and the regional level (23.4% and 20.6%, respectively). The investigation on the use of OC use before pregnancy showed that 60.9% of the women in our study used the pill before child birth with DS, while this rate is around 48.7% nationally and 59.1% regionally. The other variables studied did not show any difference between the two groups.

DISCUSSION

Maternal age at birth in our study influences DS birth. The median maternal age at DS birth was 35.95 years versus 28.49 years of non-DS (Table 1). This result was similar to that found in other studies [5, 16, 17, 18]. Likewise, the paternal age showed a statistically significant difference with DS birth in our study. This finding was agree with what does found by several studies especially when paternal age was adjusting for

Table 3. Number and percentage for modalities of qualitative variables and mean \pm standard deviation for quantitative variables of DS households studied and their comparison with data from National Moroccan Population Surveys (ENPSF, 2018, ENJ, 2011)

Variables	Modalities	Present study (%)	National data (%)	Marrakech-Safi data (%)	Survey
Woman's level of education	None	35.1	39.5	44.2	ENPSF 2018
	Primary	22.1	24.2	26.3	
	Secondary	26.5	27.5	22.4	
	Superior	16.3	8.8	7.0	
Man's level of education	None	22.7	22.7	27.4	
	Primary	22.7	29.8	31.6	
	Secondary	33.7	37.4	33.0	
	Superior	20.9	10.1	7.9	
Paid employment	Man	82.7	62.0	63.0	
	Woman	21.4	13.1	9.3	
Smokers	Man	50.8	21.9	22.4	
	Woman	0.0	1.0	1.1	
Alcohol consumption	Man	29.0	15.0	-	ENJ 2011
	Woman	0.0	0.4	-	
Mean age at first marriage (years)	Man	30.63 \pm 6.28	31.9	30.4	ENPSF 2018
	Woman	24.59 \pm 6.88	25.5	23.8	
Kinship		11.6	23.4	20.6	
Oral contraceptif use before pregnancy		*60.9	48.7	59.1	
Mean size of Moroccan households (persons)		5.42 \pm 2.02	4.5	4.9	
Mean age difference between spouses (years)		6.36 \pm 6.7	7.9	8.1	
Synthetic Fertility Index SFI (years)		1.92	2.38	-	
Mean number of live births		2.96	2.6	2.8	

SD - standard deviation , * - Down syndrome pregnancy

maternal age [19, 20, 21] and contradictory with other studies [22, 23].

The results of our study suggest a role of OC use in DS birth. These results agree with those found by Ghosh et al, who confirmed the effect of OC use in DS birth, based on observation of an increasing frequency of OC use with advancing maternal age [7]. However, our results concerning the length of OC use before pregnancy were contradictory to those reported by Nagy et al. [10]. That study suggested that for women giving birth at advanced maternal age, the history of longer OC usage before pregnancy might lower the risk of common trisomy of the fetus. Even longer oral contraception use before pregnancy in women of advanced reproductive age can reduce the risk of common fetal trisomy [12].

The rank of birth did not show significant differences for DS in our sample even though it was found that children with DS are born in the third rank on average (3.07 \pm 1.88). The study of Jaouad et al showed that 40% of DS patients were born after at least four healthy births [24].

Regarding parents sociodemographic level evaluated by the level of education and paid employment we noticed a clear difference concerning the higher level of education and high rate of people who exercise paid employment in favor of our sample. This difference may be explained by the region of residence location of the majority of the population studied in urban area. This result was contradicts with what has been shown by Hunter et al [25] that a low socio-economic level of parents increases the risk of having a child with DS.

Parental habits such as smoking cigarettes and consuming alcohol are environmental risk factors among other widely studied whose impact on DS birth was confirmed by several studies [8, 26]. Concerning our study, there was a marked increase in the consumption of cigarettes and alcohol among men compared to what is recorded at the Moroccan national level [14,15].

The rate of kinship in families studied (11.6%) was lower than that recorded at the national and the regional level (23.4% and 20.6%, respectively). This result is in agreement with several studies which have

not shown an association with DS, especially when consanguinity is evaluated alone as a risk factor [26, 27, 28], but confirmed in other studies either alone [29] or in combination with other bio-socio-demographic risk factors [6, 8].

Limitations

Limitations of our study are related to the population of studied families, without taking into account families with non-malformed children and to the small sample size. This is justified by the constraints of time and limited resources that have not allowed us to expand our research.

CONCLUSION

Our results showed that parents included in this study had a higher educational level, were more involved in paid employment and had more smokers and alcohol consumption in men. Among the risk factors studied only the maternal age at birth, the paternal age at birth and the use of oral contraception before pregnancy that have shown an association with the birth with Down syndrome.

Disclosure of interest

The authors declare that there is no conflict of interests.

Acknowledgment

We gratefully acknowledge all the parents whose participation has made this study possible. In addition, we want to thank all personnel at each visited association and health center that provide care and support for individuals with Down syndrome in Marrakech-Safi region, for helping and supporting us to complete this study. We would like to thank Mr. Harich Nourdin for reviewing this article

REFERENCES

1. Down JL. Observations of an ethnic classification of idiots. Clin Lect Rep London Hosp 1866;13:121–123. <https://doi.org/10.1192/bjp.13.61.121>.
2. Jacobs PA, Baikie AG, Court Brown WM, Strong JA. The somatic chromosomes in Mongolism. Lancet 1959;1:710. [https://doi.org/10.1016/S0140-6736\(59\)91892-6](https://doi.org/10.1016/S0140-6736(59)91892-6).
3. Lejeune J. Le Mongolisme, premier exemple d'aberration autosomique humaine. Ann Genet 1959 ;1:41–49.
4. Antonarakis SE, Down Syndrome Collaborative Group. Parental origin of the extra chromosome in trisomy 21 as indicated by analysis of DNA polymorphisms. N Engl J Med 1991;324:872–876. <https://doi.org/10.1056/NEJM199103283241302>.
5. Allen EG, Freeman SB, Druschel C, Hobbs CA, O'Leary LA, Romitti PA, et al. Maternal age and risk for trisomy 21 assessed by the origin of chromosome nondisjunction: a report from the Atlanta and National Down Syndrome Projects. Hum 2009;125:41–52. <https://doi.org/10.1007/s00439-008-0603-8>.
6. Malini SS, Ramachandra NB. Possible risk factors for Down syndrome and sex chromosomal aneuploidy in Mysore, South India. Indian Journal of Human Genetics 2007;13:102–108. <https://doi.org/10.4103/0971-6866.38984>.
7. Ghosh S, Hong CS, Feingold E, Ghosh P, Ghosh P, Bhaumik P, et al. Epidemiology of Down syndrome: New Insight Into the Multidimensional Interactions Among Genetic and Environmental Risk Factors in the Oocyte. Am J Epidemiol 2011;174(9):1009–1016. <https://doi.org/10.1093/aje/kwr240>.
8. Shalaby HMA. A study of new potential risk factors for Down syndrome in Upper Egypt. The Egyptian Journal of Medical Human Genetics 2011;12, 15–19.
9. Martínez-Frías ML, Bermejo E, Rodríguez-Pinilla E, Prieto L. Periconceptional exposure to Contraceptive Pills and Risk for Down Syndrome. Journal of Perinatology 2001;21:288 – 292. <https://doi.org/10.1038/sj.jp.7210538>.
10. Nagy GR, Györffy B, Nagy B, Rigó Jr J. Lower risk for Down syndrome associated with longer oral contraceptive use: a case-control study of women of advanced maternal age presenting for prenatal diagnosis. Contraception 2012;87:455–458. <https://doi.org/10.1016/j.contraception.2012.08.040>.
11. Ray A, Hong CS, Feingold E, Ghosh P, Ghosh P, Bhaumik P, et al. Maternal Telomere Length and Risk of Down Syndrome: Epidemiological Impact of Smokeless Chewing Tobacco and Oral Contraceptive on Segregation of Chromosome 21. Public Health Genomics 2016; 19:11–18
12. Horányi D, Babay LÉ, Rigó J Jr., Györffy B, Nagy GR: Effect of extended oral contraception use on the prevalence of fetal trisomy 21 in women aged at least 35 years. Int J Gynecol Obstet 2017; 138: 261–266
13. World Health Organization. Neonatal and Perinatal Mortality: Country, Regional and Global Estimates. Geneva, Switzerland. World Health Organization 2006. <https://apps.who.int/iris/handle/10665/43444>.
14. ENPSF. Enquête Nationale sur la Population et la Santé Familiale 2018. Ministère de la Santé Publique, Royaume du Maroc.
15. ENJ. Enquête Nationale sur les Jeunes 2011, rapport de synthèse. Haut-Commissariat au Plan. Royaume du Maroc. Accessed on 10/8/2023 https://www.hcp.ma/downloads/Enquete-nationale-sur-les-jeunes_t22388.html
16. Yoon PW, Freeman SB, Sherman SL, Taft LF, Gu Y, Pettay D, et al. Advanced Maternal Age and the Risk of Down Syndrome Characterized by the Meiotic Stage of the Chromosomal Error: A Population-Based Study. Am. J. Hum. Genet 1996; 58:628–633.
17. Gauden ME. Maternal age effect: The enigma of Down syndrome and other trisomic conditions. Mutation Research 1992;296: 69–88
18. Laignier MR, Lopes-Júnior LC, Santana RE, Leite FMC, Brancato CL. Down Syndrome in Brazil: Occurrence and Associated Factors. Int. J. Environ.

- Res. Public Health 2021;18(22), 11954; <https://doi.org/10.3390/ijerph182211954>
19. *Fisch H, Hyun G, Golden R, Hensle TW, Olsson CA, Liberson GL.* The influence of paternal age on Down syndrome. *J Urol* 2003;169:2275–2278. <https://doi.org/10.1097/01.ju.0000067958.36077.d8>.
20. *Dzurova D, Pikhart H.* Down syndrome, paternal age and education: comparison of California and the Czech Republic. *BMC Public Health* 2005;5:69 doi:10.1186/1471-2458-5-69
21. *Stene J, Stene E, Stengel-Rutkowski S, Murken JD.* Paternal Age and Down's Syndrome Data from Prenatal Diagnoses (DFG). *Hum Genet* 1981; 59:119-124
22. *Buwe A, Guttenbach M, Schmid M.* Effect of paternal age on the frequency of cytogenetic abnormalities in human spermatozoa. *Cytogenet Genome Res* 2005;111:213–228. <https://doi.org/10.1159/000086892>.
23. *Thompson JA.* Disentangling the roles of maternal and paternal age on birth prevalence of Down syndrome and other chromosomal disorders using a Bayesian modeling approach. *Thompson BMC Medical Research Methodology* 2019;19:82 <https://doi.org/10.1186/s12874-019-0720-1>.
24. *Jaouad IC, Cherkaoui Deqaqi S, Sbiti A, Natiq A, Elkerch A, Sefiani F.* Cytogenetic and epidemiological profiles of Down syndrome in a Moroccan population: a report of 852 cases. *Singapore Med J* 2010;51(2):133–136.
25. *Hunter JE, Allen EG, Shin M, Bean LJ, Correa A, Druschel C, et al.* The association of low socioeconomic status and the risk of having a child with Down syndrome: a report from the National Down Syndrome Project. *Genetics in medicine* 2013;15(9):698-705
26. *Corona-Rivera JR, Martínez-Macias FJ, Bobadilla-Morales L, Corona-Rivera A, Peña-Padilla C, Rios-Flores IM, et al.* Prevalence and risk factors for Down syndrome : A hospital-based single-center study in Western Mexico. *Am J Med Genet* 2019; 1–7
27. *Rezayat AA, Nazarabadi MH, Andalibi MS, Ardabili HM, Shokri M, Mirzaie S and Jarahi L.* Down syndrome and consanguinity. *J Res Med Sci* 2013;18:995-7.
28. *Jaouad IC, Elalaoui SC, Sbiti A, Elkerch F, Belmahi L, Sefiani A.* Consanguineous marriages in Morocco and the consequence for the incidence of autosomal recessive disorders. *J. Biosoc. Sci.* 2009;41(5):575–581
29. *Ray A, Oliver TR, Halder P, Pal U, Sarkar S, Dutta S, et al.* Risk of Down syndrome birth: Consanguineous marriage is associated with maternal meiosis-II nondisjunction at younger age and without any detectable recombination error. *Am J Med Genet* 2018;1–8.

Received: 23.08.2023

Accepted: 07.11.2023

Published online first: 24.11.2023