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Trisomy 21: Experience at the Children's Hospital of Rabat

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Abstract **Original Research Article**

***Introduction*:** Trisomy 21 is a congenital chromosomal abnormality caused by the presence of a supernumerary chromosome for the 21st pair. It is characterized by cognitive retardation associated with particular morphological changes. This is one of the most common genetic diseases, with an incidence about 1/770 births. We report a case series observed at the delivery room of Souissi Maternity Center in Rabat (Morocco) during one-year period. ***Material and methods*:** This is a prospective study of the neonatal registry during maternity consultations. All cases of trisomy 21 were recorded during the year 2015. ***Results*:** There were a total of 17257 births, with 44 cases of Trisomy 21; Resulting in an incidence of 0.25% (1 for 392 births). These were 25 males (56.81%) and 19 females (43.19%). The average age of women at the time of delivery was 34,4 ± 7 years . The most affected age group was those with an age greater than or equal to 35-year-old (23 cases) with also a significant number of cases in women under 35-year-old of age (21 cases). Consanguinity was found in only one case. There was no history of trisomy 21 in previous pregnancies. ***Conclusion*:** Trisomy 21 is quite common in our maternity. Patients' advanced age seems to be the main risk factor. However, patients under the age of 35-year-old deserve more surveillance in our context.

Keywords: Trisomy 21 – Incidence – Maternal age.

INTRODUCTION

Trisomy 21 (T21) is a congenital chromosomal anomaly caused by the presence of an extra chromosome in the 21st pair. It is one of the most common genetic disorders, with an incidence of approximately 1 in 770 births [1]. The only recognized risk factor is advanced maternal age. T21 is characterized by cognitive delay with specific morphological changes. It is often associated with certain malformations or complications, which necessitates systematic medical follow-up. Intellectual disability is usually mild, allowing for acquisition of reading skills and some degree of autonomy in mainstream settings in at least half of cases. Currently, there is no treatment for this chromosomal anomaly and its cognitive consequences, but early and lifelong multidisciplinary medical, educational, and rehabilitative support can improve their skills and, for a large proportion of individuals, achieve a certain level of autonomy in mainstream settings. Life expectancy is currently over 55 years, limited by the development of Alzheimer's-type dementia in 30 to 40% of cases.

We report cases observed during neonatal consultations at Souissi Maternity Hospital in Rabat during a one-year period (from January 1 to December 31, 2015).

MATERIALS AND METHODS

This is a prospective study evaluating the incidence of Down syndrome in the delivery room of Souissi Maternity in Rabat, Morocco, during the year 2015 and the associated risk factors.

Inclusion Criteria: All newborns with a diagnosis of Down syndrome based on typical clinical features confirmed by cytogenetic study.

Exclusion Criteria: Newborns with characteristic dysmorphic syndrome not confirmed by cytogenetics.

The incidence of Down syndrome was calculated using the formula:
Incidence = (Number of cases of Down syndrome in 2015 / Total number of births) x 100

Several risk factors were analyzed to study their implications in the incidence of Down syndrome:

- Maternal age
- Consanguinity
- History of Down syndrome
- Number of pregnancies
- Number of deliveries = Number of previous childbirths
- Maternal weight
- Maternal height
- Body mass index (BMI) = Weight / Height2
- Mode of delivery
- Sex of the newborn

Data were collected from the neonatal consultation registry at Souissi Maternity. SPSS 21.0 software was used for statistical analysis.

RESULTS

Out of a total of 17,257 births, there were 44 cases of trisomy 21, resulting in an incidence of 0.25% (1 case of Down syndrome per approximately 392 births). The mean age of the patients at the time of delivery was 34.4 years ± 7 years. The age group most affected was patients aged 35 years or older (23 cases), with a significant number of cases also observed in women under 35 years old (21 cases). Consanguinity was found in only one case, and there were no previous history of trisomy 21 in previous pregnancies. The rest of the data is detailed in Table 1.

Table 1: Characteristics of parturients, (N = 44)

Characteristics	values
Age : • > ou = 35 ans • < 35 ans : * 24-34 ans * < 24 ans	34,4 ± 7 ans 23 (52,3%) 21 (47,7%) 16 (36,4%) 5 (11,3%)
Inbreeding	1 (2,3%)
History of T21 during previous pregnancies	0
Weight	81,2 ± 8,6 kg
Size	162,2 ± 4,7 cm
Body mass index	30,9 ± 2,5 kg/m^2
Number of pregnancies	2,8 ± 1,4
Number of parity	2,4 ± 1,5

Regarding newborns with trisomy 21, 25 (56.8%) were male, while 19 (43.2%) were female. They were delivered vaginally in 34 cases (77.3%), while cesarean section was performed in 10 cases (22.7%). Two newborns died 1 hour after birth in the delivery room due to neonatal distress. These data are detailed in Table 2.

Table 2: Characteristics of newborns with trisomy 21 (N = 44)

Characteristics	Values
Delivery : • Normal • Cesarean section	 34 (77,3%) 10 (22,3%)
Gender : • Male • Female	 25 (56,8%) 19 (43,2%)
Survival : • Alive • Dead	 42 (95,5%) 2 (4,5%)

DISCUSSION

Trisomy 21 is the most common chromosomal anomaly responsible for intellectual disability. In the absence of prenatal screening, it would account for approximately 10% of intellectual disabilities, with a frequency of about 1 in 770 births [1]. The screening for this syndrome raises ethical questions, particularly in terms of information, so that each pregnant woman can make a choice that aligns with her personal beliefs.

In our series, the incidence is twice as high compared to international values [2]. This can be explained by the fact that in most European countries, prenatal screening has led to a 50% decrease in trisomy 21 births. Only Ireland and Malta have similar incidences to our series; this can be explained by the fact that the current legislation in these conservative countries does not allow for abortion. In our context,

the majority of births at the Souissi maternity ward are the result of poorly or non-followed pregnancies.

Regarding risk factors, maternal age remains the only established causal factor with demonstrated responsibility in Down syndrome (T21). This relationship was described by Penrose over 60 years ago, well before the genetic basis of T21 was elucidated [3]. In fact, the incidence increases from 1 in 1528 births at the age of 20 to 1 in 118 births at the age of 40 [4]. This is consistent with the results of our study, which reveals a high rate of T21 in mothers over the age of 35. However, there is also a significant number of T21 cases in younger mothers under the age of 35 (21 cases), which should prompt further epidemiological studies in this population to determine potential risk factors that may be involved.

Despite these scientific advances, the biological basis of the maternal age effect remains unclear. Studies on the parental origin of aneuploidies show that the effect of maternal age is related to errors of maternal origin and not paternal origin. It is evident, therefore, that the ovary, and not the uterus, is the source of this effect. Several hypotheses have been proposed, including a decrease in the frequency of oocyte chiasmata with age [5], a decrease in selection against aneuploid oocytes with age [6], a decrease in the pool of mature oocytes with age [7], changes in meiotic cell cycle with age [8], or changes in follicular microenvironment [9].

In addition to maternal age, a large number of genetic and environmental factors have also been implicated in predisposition to T21. These factors include consanguinity [10], parental irradiation [11], maternal diabetes [12], oral contraceptives [13], anti-thyroid antibodies [14], parity [15], and certain genetic [16] or chromosomal [17] polymorphisms. However, none of these associations have been convincingly established. Nevertheless, some factors deserve further attention. For instance, as early as 1985, Warburton [18] showed that when a mother of a child with Down syndrome is under the age of 30, there is an increased risk for her to have another child with Down syndrome. This risk is particularly evident below the age of 30, when the proportion of trisomies due to the maternal age effect is low.

More recently, an association between folate metabolism and trisomy 21 has been identified. A study has shown an increased frequency of a polymorphism of methylenetetrahydrofolate reductase (MTHFR 677 C -> T) in mothers of trisomic children [19]. Another study, focusing on the MTRR 66A -> C polymorphism of another enzyme in folate metabolism, methionine synthase reductase, confirmed this finding [20].

Lastly, a recent case-control study showed an association between active smoking and trisomy 21 resulting from a second meiotic division error [21]. Surprisingly, this association was only observed in women under the age of 35. Furthermore, combined oral contraceptive use and smoking significantly increased this association.

CONCLUSION

Trisomy 21 is relatively common in our context in the absence of organized prenatal screening. Advanced maternal age appears to be the main risk factor. However, younger patients under the age of 35 deserve more surveillance in our context. Antenatal care for these patients becomes a necessity, and our study can serve as a foundation for further larger-scale epidemiological studies to implement a national screening plan for T21.

Contribution of Authors: All authors contributed to the conception of this article

REFERENCES

1. Ayme, S. (1996). Value of registries in decision making in public health: the example of trisomy 21. *Revue D'epidemiologie et de Sante Publique*, *44*, S82-89.
2. Loane, M., Morris, J. K., Addor, M. C., Arriola, L., Budd, J., Doray, B., ... & Dolk, H. (2013). Twenty-year trends in the prevalence of Down syndrome and other trisomies in Europe: impact of maternal age and prenatal screening. *European Journal of Human Genetics*, *21*(1), 27-33.
3. 3 - Penrose L. The relative effects of paternal and maternal age in mongolism. J Genet. 1933 ; 27: 219-24.
4. Hassold, T., & Chiu, D. (1985). Maternal age-specific rates of numerical chromosome abnormalities with special reference to trisomy. *Human genetics*, *70*, 11-17.
5. Henderson, S. A., & Edwards, R. G. (1968). Chiasma frequency and maternal age in mammals. *Nature*, *218*(5136), 22-28.
6. Zheng, C. J., & Byers, B. (1992). Oocyte selection: a new model for the maternal-age dependence of Down syndrome. *Human genetics*, *90*, 1-6.
7. Warburton, D. (1989). The effect of maternal age on the frequency of trisomy: change in meiosis or in utero selection?. *Progress in Clinical and Biological Research*, *311*, 165-181.
8. Eichenlaub-Ritter, U., & Boll, I. (1989). Nocodazole sensitivity, age-related aneuploidy, and alterations in the cell cycle during maturation of mouse oocytes. *Cytogenetic and Genome Research*, *52*(3-4), 170-176.
9. Gaulden, M. E. (1992). Maternal age effect: the enigma of Down syndrome and other trisomic conditions. *Mutation Research/Reviews in Genetic Toxicology*, *296*(1-2), 69-88.
10. Alfi, O. S., Chang, R., & Azen, S. P. (1980). Evidence for genetic control of nondisjunction in

man. *American Journal of Human Genetics*, *32*(4), 477-483.
11. Uchida, I., & Curtis, E. (1961). A possible association between maternal radiation and mongolism. *Lancet (England)*, *2*, 848-850.
12. Narchi, H., & Kulaylat, N. (1997). High incidence of Down's syndrome in infants of diabetic mothers. *Archives of disease in childhood*, *77*(3), 242-244.
13. Harlap, S., Shiono, P., Pellegrin, F., Golbus, M., Bachman, R., Mann, J., ... & Lewis, J. P. (1979). Chromosome abnormalities in oral contraceptive breakthrough pregnancies. *The Lancet*, *313*(8130), 1342-1343.
14. Torfs, C. P., Van den Berg, B. J., Oechsli, F. W., & Christianson, R. E. (1990). Thyroid antibodies as a risk factor for Down syndrome and other trisomies. *American journal of human genetics*, *47*(4), 727-734.
15. Zheng, C. J., & Byers, B. (1992). Oocyte selection: a new model for the maternal-age dependence of Down syndrome. *Human genetics*, *90*, 1-6.
16. Antonarakis, S. E., Kittur, S. D., Metaxotou, C., Watkins, P. C., & Patel, A. S. (1985). Analysis of DNA haplotypes suggests a genetic predisposition to trisomy 21 associated with DNA sequences on chromosome 21. *Proceedings of the National Academy of Sciences*, *82*(10), 3360-3364.
17. Jackson-Cook, C. K., Flannery, D. B., Corey, L. A., Nance, W. E., & Brown, J. A. (1985). Nucleolar organizer region variants as a risk factor for Down syndrome. *American journal of human genetics*, *37*(6), 1049-1061.
18. Warburton, D. (1985). Genetic factors influencing aneuploidy frequency. *Aneuploidy: etiology and mechanisms*, 133-148.
19. James, S. J., Pogribna, M., Pogribny, I. P., Melnyk, S., Hine, R. J., Gibson, J. B., ... & Gaylor, D. W. (1999). Abnormal folate metabolism and mutation in the methylenetetrahydrofolate reductase gene may be maternal risk factors for Down syndrome. *The American journal of clinical nutrition*, *70*(4), 495-501.
20. Hobbs, C. A., Sherman, S. L., Yi, P., Hopkins, S. E., Torfs, C. P., Hine, R. J., ... & James, S. J. (2000). Polymorphisms in genes involved in folate metabolism as maternal risk factors for Down syndrome. *The American Journal of Human Genetics*, *67*(3), 623-630.
21. Yang, Q., Sherman, S. L., Hassold, T. J., Allran, K., Taft, L., Pettay, D., ... & Freeman, S. B. (1999). Risk factors for trisomy 21: Maternal cigarette smoking and oral contraceptive use in a spopulation-based case-control study. *Genetics in Medicine*, *1*(3), 80-88.