



Predictive Factors for Pregnancy Termination Following a Prenatal Diagnosis of Down Syndrome: Experience from the Reunion Registry of Congenital Malformations from 2002 to 2015

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Introduction

The generalized screening and Prenatal Diagnosis (PND) of Down Syndrome (DS), which is responsible for intellectual disability, have been used in France since 2002 [1]. The Reunion, a French island located in the Indian Ocean, has an extremely diverse population in terms of its ethnicity, culture, and religion. The island is also characterized by large socioeconomic and environmental disparities.

According to the data from French Congenital Malformation Registry, the prevalence of DS (live births and medical termination of pregnancy) in Reunion Island was the lowest in France in 2017 (23.04 per 10,000 births), notably due to the young maternal age [2]. However, in terms of live births, Reunion Island has the highest prevalence of DS in France (12.24 vs. 5.81 per 10,000 births) despite well-organized PND. In fact, the use of Termination of Pregnancy for Fetal Abnormality (TOPFA) is the lowest in France (10.8 vs. 26.3 per 10,000 births) [2]. Thus, this first exploratory retrospective study aimed to identify the predictive factors of TOPFA in mothers of fetuses with a PND of DS living on Reunion Island to better understand this Reunionese paradox.

Methods

This retrospective study included all women living on Reunion Island with a positive PND of DS during their pregnancy from 2002 to 2015.

These data are taken from the official database of the Reunion Registry of Congenital Malformations (REMACOR), approved by the French Public Health Agency, which continuously and exhaustively registers cases of malformations and chromosomal anomalies on Reunion Island. Cases can be identified through active searching or reporting from various sources: Maternity and hospital wards as well as the Medical Informatics Department. All data were retrieved from medical records. A midwife trained in clinical research and data collection entered the data into the software Eurocat Data Management Program [3].

Variables available in REMACOR included the characteristics of the pregnancy and fetus (TOPFA, gestational age at diagnosis, length of gestation, sex, birth weight), characteristics of the parents (age, mother's place of residence), and gynecological history of the mother. The maternal place of residence was determined based on five inter communal territories of Reunion Island [4]. Continuous variables were described using median and inter quartile range values and categorical variables as percentages. Comparisons between TOPFA and no TOPFA used the Mann-Whitney U test or Chi² or Fisher's exact test, as appropriate. Two-sided tests and a significance threshold of $p \leq 0.05$ were used. A multivariable logistic regression model was used to identify factors associated with TOPFA. Variables were selected based on the literature (two forced variables), those with a low rate of missing data (<20%) or a low correlation. All statistical analyses were performed using SAS[®] (v9.4, SAS Institute, Cary, NC, USA, 2013) software.

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Table 1: Characteristics of pregnancies, fetuses with DS, parents, and factors associated with TOPFA in the REMACOR (n=321, Reunion Island, 2002-2015).

		n (%) or median (IQR) N=321	No TOPFA N=89 n (%) or median (IQR)	TOPFA N=232 n (%) or median (IQR)	p-value*	ORa (95% CI) Multivariate
Characteristics of pregnancies and fetuses with DS by PDN						
Gestational age at diagnosis, weeks	n=318	16.0 (13.0-20.0)	17.0 (15.5-22.0)	15.0 (13.0-19.0)	<0.001	0.89 (0.85-0.95)
≥ 15 weeks		206 (64.8)	70 (79.5)	136 (59.1)	0.001	
Length of gestation, weeks	n= 320	22.0 (19.0-35.0)	38.0 (36.0-38.0)	20.0 (18.0-23.0)	<0.001	
≥ 15 weeks [†]		297 (92.8)	89 (100.0)	208 (90.0)	0.001	
Male sex	n=320	178 (55.6)	46 (51.7)	132 (57.1)	0.379	
Birth weight, grams	n=310	495 (250-213)	2710 (2300-3155)	330.0 (198.0-580.0)	<0.001	
≥ 500 grams [†]		155 (50.0)	86 (96.6)	69 (31.2)	<0.001	
Characteristics of parents						
Mother's age at delivery, years	n=321	38 (33-41)	38.0 (33.0-41.0)	38.0 (33.0-40.0)	0.667	1.06 (1.01-1.11)
Father's age at delivery, years	n=238	39 (34-44)	39.0 (31.0-43.0)	39.0 (34.0-44.0)	0.751	
Mother's place of residence	n=320				0.266	
CINOR		78 (24.4)	18 (20.2)	60 (26.0)		1
CASUD		60 (18.8)	21 (23.6)	39 (16.9)		0.44 (0.19-1.03)
CIREST		39 (12.2)	8 (9.0)	31 (13.4)		1.18 (0.41-3.38)
CIVIS		84 (26.2)	28 (31.5)	56 (24.2)		0.43 (0.19-0.96)
TCO		59 (18.4)	14 (15.7)	45 (19.5)		0.77 (0.31-1.89)
Maternal gynecological history						
Number of previous pregnancies	n=314	2.0 (1.0-4.0)	3.0 (1.0-4.0)	2.0 (1.0-3.0)	0.014	
0		50 (15.9)	13 (14.9)	37 (16.3)		
1-3		176 (56.1)	41 (47.1)	135 (59.5)	0.05	
≥ 4		88 (28.0)	33 (37.9)	55 (24.2)		
Number of previous spontaneous abortions	n=314	-	-	-	-	
0		218 (69.4)	61 (70.1)	157 (69.2)		
1		59 (18.8)	18 (20.7)	41 (18.1)	0.63	
≥ 2		37 (11.8)	8 (9.2)	29 (12.8)		
Previous induced abortions [†]	n=315	20 (6.3)	3 (3.4)	17 (7.5)	0.3	
Number of previous live births	n=318	1.0 (1.0-3.0)	2.0 (1.0-4.0)	1.0 (0.0-2.0)	<0.001	0.69 (0.59-0.82)
0		78 (24.5)	16 (18.2)	62 (27.0)		
1		84 (26.4)	16 (18.2)	68 (29.6)		
2		65 (20.4)	15 (17.0)	50 (21.7)	<0.001	
3		41 (12.9)	15 (17.0)	26 (11.3)		
≥ 4		50 (15.7)	26 (29.6)	24 (10.4)		

*p-value refers to comparisons between no-TOPFA and TOPFA using a Mann-Whitney test for continuous variables and Chi² test or Fisher's exact test (†) for categorical variables

CASUD: Intermunicipal Community of Southern Area; CINOR: Intermunicipal Community of Northern Reunion; CIREST: Intermunicipal Community of Eastern Reunion; CIVIS: Intermunicipal Community of the Solidarity Cities; 95% CI: 95% Confidence Interval; DS: Down Syndrome; IQR: Interquartile Range; ORa: Adjusted Odds Ratio; PDN: Prenatal Diagnosis; REMACOR: Reunion Registry of Congenital Malformations; TCO: West Coast Territory; TOPFA: Termination of Pregnancy for Fetal Abnormality

Results

Between 2002 and 2015, 404 DS were registered in the REMACOR database. Among these 404 DS cases, 83 did not have a PDN, resulting in 82 live births and 1 fetal death. Thus, 321 DS with PDN were included in the study. Among them, 232 women (72.3%) chose to Terminate Their Pregnancy (TOPFA). Results are presented in Table 1. In the Reunionese population, TOPFA was associated with early gestational age at DS diagnosis (ORa=0.89; CI95%: (0.85-0.95), higher maternal age at delivery (ORa=1.06; CI95%: (1.01-1.11), living in the CINOR compared to the CIVIS intermunicipal community (ORa=0.43; CI 95%: (0.19-0.96), and having fewer previous live births

(ORa=0.69; CI 95%: (0.59-0.82)).

Discussion

On Reunion Island, approximately three-quarters of women chose to terminate their pregnancy when DS was diagnosed, which is close to the rate observed in England and the Netherlands but very low compared to mainland France [1]. Factors associated with TOPFA in our population were very similar to those reported in the literature [5,6]. Our results highlight that the mother's place of residence has an impact on TOPFA in Reunion Island. However, we believe that the information delivered during prenatal and preconceptional genetic counseling is performed identically between the two physical sites

(north and south) of the island's university hospital, because these two entities are part of the same hospital center that uses homogeneous procedures, regardless of the physical site of the institution. On the other hand, the north of the island, which includes the island's capital (Saint Denis), has many jobs in the tertiary sector, whereas the south of the island is much more marked by jobs in the primary sector (agriculture) and the active practice of ancestral cultural traditions. Thus, the CIVIS territory is marked by a high level of precarity, which indirectly highlights the influence of socioeconomic level on the TOPFA [7]. Other variables such as ethnicity, religion, support network, perceived family approval, and perceived burden of care would be interesting to explore, although they are not collected in the registry. In fact, solidarity within Creole families and high religiosity may promote the acceptance of a child with DS in Reunion Island. However, quantitative studies do not explain decision-making, which is a complex, multifactorial, and individualized process, nor do they explore why and how certain factors are important and may have different meanings in different contexts. For this reason, we intend to conduct a qualitative study of couples to explore their reasons and motivations for not undergoing a TOPFA (<https://clinicaltrials.gov/ct2/show/NCT04811534>).

Ethics Approval

The Reunion Registry of Congenital Malformations (REMACOR) oversees the surveillance of congenital malformations for public health and research purposes. It is declared to the French “Commission Nationale de l’Informatique et des Libertés” (CNIL) according to the authorization N°909410.

Author’s Contribution

HR designed and supervised the study; BNN investigated and collected the data; VL conducted the statistical analysis; LB, VL, NI drafted the article. In addition, all authors have contributed substantially to the interpretation of results and provided critical revision of the manuscript for important intellectual content. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the version to be published.

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