

EPIDEMIOLOGICAL AND CLINICAL PROFILE OF NEWBORNS WITH TRISOMY 21 IN MOROCCO: A FIVE-YEAR PERIOD STUDY

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Abstract

Introduction: Trisomy 21 is the most common chromosomal abnormality with a prevalence of 1/700 to 1/1000 live births. In Morocco, epidemiological data remains limited. This study aimed to describe the epidemiological and clinical profile of patients with trisomy 21 in the Rabat region over five years. **Materials and Methods:** This was a retrospective descriptive and analytic study of two complementary cohorts: one cohort of patients followed in outpatient consultation and one cohort of newborns diagnosed in the delivery room. Demographic, clinical data and comorbidities were analyzed using SPSS version 26.0. **Results:** The total population studied included 136 patients with 50.7% male newborns. Congenital hypothyroidism was the most frequent associated comorbidity (55.9%), followed by congenital heart disease (6.5%). Consultations paradoxically increased during the COVID-19 pandemic (33 in 2020, 105 in 2022). The mean maternal age in the neonatal cohort varied from 39.5 years in 2021 (100% ≥ 35 years) to 32.8 years in 2023. **Conclusion:** The high prevalence of congenital hypothyroidism and the low rate of documented heart disease suggest the need to adapt screening protocols to the Moroccan context. The impact of the COVID-19 pandemic revealed vulnerabilities in access to care, particularly for young mothers. Systematic screening for comorbidities and a multidisciplinary approach are essential to optimize care.

Keywords: Trisomy 21, Down syndrome, epidemiology, Morocco, comorbidity

Introduction

Trisomy 21, also known as Down syndrome, is the most common chromosomal abnormality, with an estimated global prevalence between 1/700 and 1/1000 live births [1,2]. This pathology is characterized by the presence of a supernumerary chromosome 21, resulting in a recognizable clinical phenotype and various comorbidities that require early and multidisciplinary management [3].

Genetically, there are three types of chromosomal abnormalities responsible for trisomy 21: free homogeneous trisomy 21 (90-95% of cases), translocations (1-7% of cases), and mosaicism (1-7% of cases) [4].

The clinical characteristics of trisomy 21 include muscular hypotonia, distinctive facial features, cardiac, digestive and endocrine abnormalities, as well as variable psychomotor developmental delay [4]. Among frequently associated comorbidities, congenital hypothyroidism and congenital heart disease represent the main concerns in the neonatal period and significantly influence longterm prognosis [5,6].

In Morocco, as in many developing countries, epidemiological data concerning trisomy 21 remain limited [7]. Challenges related to early diagnosis, access to specialized care, and longterm management are considerable in this context. Moreover, cultural and socioeconomic factors can influence the care pathway of these patients [8].

The period 2020-2024 was marked by the COVID-19 pandemic, which significantly impacted health systems worldwide, including in Morocco [9]. Restrictions, hospital service reorganizations, and reduction of non-urgent consultations may have affected the diagnosis, follow-up, and management of children with trisomy 21 [10].

The main objective of this study was to describe the epidemiological and clinical profile of newborns with trisomy 21 in the Rabat region over a five-year period. The secondary objectives were to identify the demographic characteristics of the studied population, determine the prevalence of main associated comorbidities, analyze the temporal evolution of cases and the impact of the COVID-19 pandemic, and evaluate the management modalities and their evolution over the study period.

Materials and Methods

This is a retrospective descriptive and analytical study of all cases of trisomy 21 diagnosed and followed in the national reference center for neonatology and nutrition and the delivery room of the Souissi Maternity of University Hospital Center (UHC) Rabat, between January 2020 and December 2024. Inclusion criteria included all newborns with a diagnosis of trisomy 21, based on clinical and/or cytogenetic criteria, born or managed in the hospital center during the study period. The clinical diagnosis was based on the presence of typical phenotypic characteristics of trisomy 21, including muscular hypotonia, oblique palpebral fissures upward and outward, and epicanthus, flat face, short neck, short and wide hands with clinodactyly of the fifth finger and single palmar crease [4]. Exclusion criteria included children with other chromosomal aneuploidies such as trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome) and cases with incomplete files. Data were systematically extracted from medical records using a standardized protocol. Our study was based on two complementary cohorts: This cohort included all patients followed in consultation at the National Reference Center for Neonatology and Nutrition of the Children's Hospital of Rabat with the diagnosis of trisomy 21 between 2020 and 2024. The data collected included:

- Identification: File number, last name, first name
- Demographic data: Gender, place of residence, contact telephone
- Clinical data: Consultation dates, anthropometric measurements (weight, height, head circumference)
- Diagnosis and comorbidities: Type of trisomy 21, presence of congenital hypothyroidism, heart disease, digestive malformations, other abnormalities

This specific cohort included newborns diagnosed with trisomy in the delivery room of the Souissi maternity during the same period. For these cases, we had more detailed information on:

Birth context:

- Precise maternal age
- Mode of delivery (cesarean section [CS] or vaginal delivery [VD])
- Date and month of birth

Immediate outcome:

- Released to parents
- Hospitalized in neonatal intensive care
- Referred to kangaroo unit (KU)
- Hospitalized in postpartum wards

The organization of care in the institution is structured around three levels:

Level 1 (Initial Diagnosis): Concerns births at the maternity with clinical diagnosis declared by pediatricians. Newborns in good general condition are released to their mothers with prescription of a malformative assessment (Thyroid assessment at Day 3 of life, abdominalrenal ultrasound at Day 5 of life, echocardiography, transfontanellar ultrasound, karyotype), an appointment for consultation at the day hospital in the pediatric department. Mothers and their newborns can be hospitalized in the postpartum departments or at the kangaroo unit (KU).

Level 2 (Complicated Cases): Newborns presenting serious complications are referred to the neonatal intensive care department.

Level 3 (Ambulatory Follow-up): Follow-up in consultation from birth to early childhood for all children with trisomy 21 in the region.

Data were analyzed using SPSS software version 26.0. Qualitative variables were expressed as frequencies and percentages, while quantitative variables were presented as means and standard deviations or medians and interquartiles according to their distribution. Bivariate analysis used the Chi-square test or Fisher's exact test for qualitative variables, and Student's t-test or MannWhitney test for quantitative variables. A statistical significance threshold of $p < 0.05$ was retained for all analyses. All data were anonymized to preserve patient confidentiality. No informed consent was required due to the retrospective nature of the study, in accordance with institutional regulations.

Results

The study identified 136 patients between 2020 and 2024, revealing a sex distribution with slight male predominance: 69 boys (50.7%) versus 59 girls (43.4%), with 8 cases of unspecified sex (5.9%). This distribution aligned with international literature data reporting sex ratios varying between 1.04 and 1.3 in favor of boys (Figure 1).

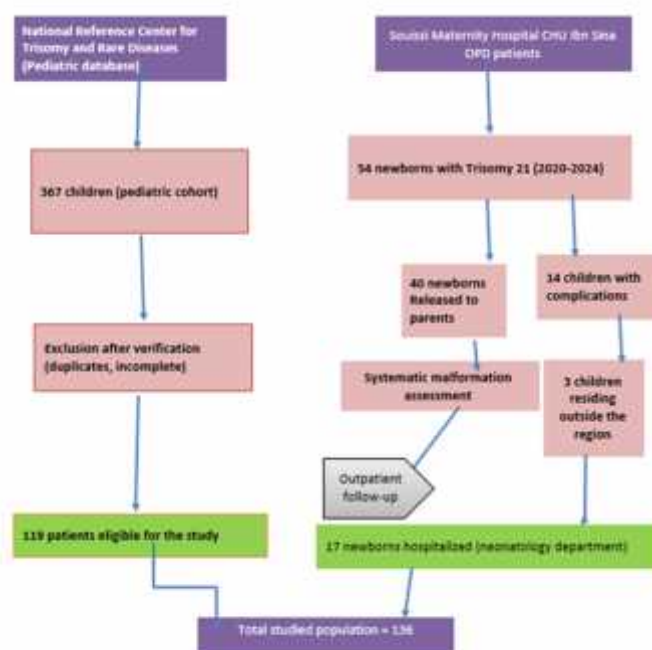


Figure 1: Flow chart of the studied population with trisomy 21 (2020-2024).

Analysis of the hospital prevalence of trisomy 21 over the period 2020-2024 revealed significant variations from year to year. The average

prevalence over the five years was 1.01 per 1000 births, with a minimum of 0.59% in 2021 and a maximum of 1.46% in 2024 (Table I).

Table I.: Hospital prevalence of trisomy 21 by year (2020-2024)

Year	Deliveries	T21 Cases	Prevalence (%)	Prevalence (%)	95% CI
2020	12,861	16	1.24	0.124	[0.71-2.01]
2021	10,198	6	0.59	0.059	[0.22-1.28]
2022	11,072	9	0.81	0.081	[0.37-1.54]
2023	10,444	10	0.96	0.096	[0.46-1.76]
2024	8,877	13	1.46	0.146	[0.78-2.50]
Total	53,452	54	1.01	0.101	[0.76-1.31]

The main comorbidities associated with trisomy 21 in our cohort are presented in Table II. Congenital hypothyroidism was by far the most frequent comorbidity, present in 55.9% of patients (76

cases). Congenital heart disease constituted the second most frequent comorbidity, affecting 6.5% of patients (9 cases) (Table II).

Table II: Main comorbidities associated with trisomy 21 (n=136)

Comorbidity	Frequency	Percentage (%)
Congenital hypothyroidism	76	55.9
Congenital heart disease	9	6.5
Atrioventricular canal	3	2.2
Ventricular septal defect	2	1.5
Patent ductus arteriosus	2	1.5
Unspecified heart disease	2	1.5
Intrauterine growth restriction	3	2.2
Anorectal malformations	2	1.5
Epilepsy	2	1.5
Hydrocephalus	1	0.7
Isolated trisomy 21	43	31.6

Analysis of the annual distribution of trisomy 21 cases over the period 2020-2024 revealed a characteristic U-shaped trend. The number of cases experienced a significant drop in 2021 with 6 cases (11.5%), representing a 62.5% decrease compared to the 16 cases (30.8%) recorded in 2020. This significant decline coincided with the most restrictive period of the COVID-19 pandemic in Morocco.

A progressive recovery then began: 9 cases in 2022 (17.3%), 10 cases in 2023 (19.2%), reaching 13 cases in 2024 (25.0%) (Figure 2).



Figure 2: Evolution of the number of trisomy 21 cases (2020-2024)

The analysis of average maternal age by year reveals a remarkable evolution. Starting from 34.0 years in 2020, the average age jumped to 39.5 years in 2021 and 39.6 years in 2022, before dropping sharply to 32.8 years in 2023 and rising slightly to 35.1 years in 2024 (Figure 3).

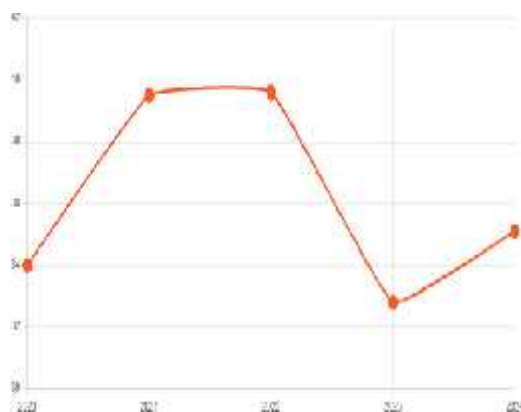


Figure 3: Average maternal age by year

The monthly distribution of cases over the entire period shows notable seasonal variations. The months of February and July show the highest frequencies with 8 cases each (15.4%), followed by March and October with 7 cases each (13.5%). Conversely, September recorded only one case (1.9%) over the five years.

This distribution suggests conception peaks in May-June and October-November, although the relatively small sample limits the scope of this observation (Figure 4).



Figure 4: Cumulative monthly distribution of trisomy 21 cases (2020-2024, n=52)

The analysis of the annual distribution of consultations over the period 2020-2024 reveals a paradoxical trend. The number of consultations shows an increase during the pandemic: 33 consultations in 2020, 60 in 2021, a peak of 105 in 2022, then 80 in 2023 and 33 in 2024 (partial data). This distribution suggests conception peaks in May-June and October-November, although the relatively small sample limits the scope of this observation. For the neonatal cohort (n=17), the annual distribution shows: 5 cases in 2021, 4 cases in 2022, 2 cases in 2023, and 6 cases in 2024. The average maternal age shows significant variations: 39.5 years in 2021 with 100% of mothers aged 35 years and over, 39.6 years in 2022, a drop to 32.8 years in 2023, then a rise to 35.1 years in 2024.

The analysis of management modalities for newborns with trisomy 21 showed a significant evolution during the study period. This evolution reflects a progressive standardization of management protocols, with better categorization of care levels required according to the severity of comorbidities and the clinical condition of the newborn (Table III).

Table III: Evolution of management modalities (2020-2024)

Management Modality	2020	2021	2022	2023	2024
Released to parents	9 (56.3%)	5 (83.3%)	4 (44.4%)	1 (10.0%)	4 (30.8%)
Hospitalized in NICU	3 (18.8%)	1 (16.7%)	3 (33.3%)	4 (40.0%)	2 (15.4%)
Referred to kangaroo unit	–	–	2 (22.2%)	–	4 (30.8%)
Postpartum services	–	–	–	5 (50.0%)	3 (23.1%)
Others	4 (25.0%)	–	–	–	–

Discussion

Our study of 136 patients with trisomy 21 in the Rabat region constituted one of the largest cohorts described in Morocco. The slight male predominance observed (50.7%) was consistent with international literature data reporting a sex ratio varying between 1.04 and 1.3 in favor of boys [11, 12]. The geographical concentration of cases in urban areas raised important questions about access to care, probably reflecting disparities in access to diagnosis and specialized care rather than the actual distribution of the disease [13]. In contrast to these expected demographic patterns, the exceptionally high prevalence of congenital hypothyroidism in our cohort (55.9%) contrasted sharply with international data reporting rates varying between 4% and 18% in patients with trisomy [14, 15]. This marked difference could be explained by several interconnected factors including recruitment bias, genetic factors specific to the Moroccan population, and environmental factors. Notably, Morocco adopted universal salt iodization (USI) in 1995 following WHO recommendations as a strategy to prevent and control iodine deficiency disorders [16]. However, studies indicate that despite these policies, only 25% of Moroccan households use iodized salt effectively, with only 4.5% of salt samples meeting regulatory standards [16]. Consequently, the persistently high rates of hypothyroidism in our cohort may reflect ongoing challenges with the iodine supplementation program's implementation and effectiveness. Conversely, the rate of congenital heart disease of 6.5% in our cohort was remarkably low compared to the 40-60% reported in international literature [5, 17]. This major discordance strongly suggested underdiagnosis of cardiac malformations, particularly asymptomatic or less severe forms. Limited access to systematic echocardiography was probably the main factor, as this practice was not systematically applied in our center [3]. Furthermore, the paradoxical evolution of the number of consultations during the pandemic deserved careful analysis. The increase in consultations from 33 in 2020 to 105 in 2022, despite health restrictions, could reflect a catch-up effect and increased parental awareness regarding the health of their vulnerable children [18, 19]. Additionally, the analysis of the evolution of management modalities reveals a progressive but significant transformation of the care pathway. The decrease in the percentage of newborns directly released to parents (from 56.3% in 2020 to 10% in 2023) suggests a more cautious and systematic approach in initial evaluation. Similarly, the emergence

of new management modalities (kangaroo unit from 2022, increased use of postnatal hospitalization services in 2023-2024) demonstrates a diversification and specialization of care. This evolution is positive as it allows better adequacy between the specific needs of each newborn and the level of care required.

Nevertheless, the increase in hospitalizations in neonatal intensive care (from 18.8% in 2020 to 40% in 2023) could reflect either earlier detection of complications, or a real increase in case severity, possibly linked to environmental factors or changes in obstetric practices.

Study Limitations

This retrospective study presented methodological limitations inherent to its design. Data incompleteness and selection bias linked to tertiary recruitment compromised external validity. The absence of systematic cytogenetic confirmation prevented molecular characterization of chromosomal variants. Additionally, the COVID-19 pandemic represents a significant source of bias in our study, affecting healthcare access patterns, diagnostic procedures, and population behavior during the study period. The pandemic's impact on healthcare utilization, delayed diagnoses, and altered referral patterns may have systematically influenced our findings and their generalizability to non-pandemic periods.

Implications for Practice and Perspectives

Our results highlight several priorities for improving the management of trisomy 21 in Morocco:

- **Strengthening comorbidity screening:** The establishment of standardized protocols systematically including echocardiography, thyroid assessment and ENT evaluation is essential. The high prevalence of hypothyroidism in our cohort justifies particularly vigilant screening for this comorbidity.
- **Improving access to care in rural areas:** Specific strategies must be developed to reduce the geographical disparities observed, including telemedicine and mobile consultations.
- **Continuing education for healthcare professionals:** The apparent underdiagnosis of heart disease suggests a need for continuing education, particularly in pediatric echocardiography and recognition of subtle clinical signs.

- **Development of genetic counseling:** The establishment of accessible genetic counseling consultations would improve family information and family planning, particularly important given the high maternal age observed.
- **Implementation of a national registry:** The creation of a national trisomy 21 registry would allow better epidemiological monitoring and evaluation of intervention effectiveness.
- **Research on local genetic and environmental factors:** Complementary studies are necessary to understand the high prevalence of hypothyroidism and explore risk factors specific to the Moroccan population.

Conclusion

This analysis of 136 patients with trisomy 21 revealed major epidemiological particularities in the Moroccan context: exceptionally high prevalence of hypothyroidism (55.9%), apparent underdiagnosis of heart disease (6.5%), and overall hospital prevalence of 1.01 per 1000 births. These results called for an urgent revision of neonatal screening and management protocols, with priority given to early diagnosis, systematic thyroid and cardiac screening, as well as the development of strategies to improve access to care in rural areas. The establishment of a national trisomy 21 registry and the development of genetic counseling represent absolute priorities for optimizing the management of this pathology in Morocco.

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