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# PREVALENCE OF NEURAL TUBE CLOSURE DEFECTS AND THE ORO-FACIAL CLEFTS, DURING THREE CONSECUTIVE YEARS (2012-2014) IN 20 PUBLIC HOSPITALS IN MOROCCO

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## ABSTRACT

**Background:** Closure of the neural tube defects and orofacial clefts are an important cause of mortality and neonatal morbidity among children. The objective of this work is to produce objective data on the current situation of these birth defects in Morocco. **Methods:** It is a prospective, multicentric study with duration of 36 months. It was conducted across 20 Morocco public hospitals and it involved neural tube closure defects and orofacial clefts**. Results:** Five hundred and twenty six (526) malformations were collected from 774 538 (94.55%) live births during the period 2012- 2014. They include the closure of neural tube defects (63%) and oral-facial clefts (37%). The total prevalence of all malformations is 6.79 per 10 000 live births. The most frequent anomalies in our study were as spina bifida, anencephaly and cleft lip and palate respectively prevalence de1.91 / 10 000 2.35 / 10 000), and 1.19 / 10 000 live births. Our results revealed a decrease in annual rates of malformed in general and closed neural tube defects

in particular respectively from 8.18 to 4.80 and 5.05 to 3.50 during the period 2012-2014 and a statistically significant differences in the regional distribution of these anomalies. **Conclusions:** This study can be used to evaluate the national strategy to prevent birth defects. It also provides valuable data on the current situation of these anomalies in our context.

**KEYWORDS:** Closure of neural tube defects, oral-facial clefts, prevalence, birth defects.

## INTRODUCTION

Neural tube closure anomalies and oro-facial malformations are congenital malformations resulting respectively from neural tube defects (NTDs) of variable extent during the fourth week of embryonic development and poor closing of certain parts of the face during embryonic development. On the one hand, it constitutes a real public health problem at the global level, given their importance as a cause of morbidity, stillbirth and neonatal mortality. On the other hand, it represents a socio-economic burden following disability impeding effective participation of the subject reached and causing long-term disabilities having a significant impact for these patients, their families, healthcare systems and society.[1]

Neural tube closure anomalies account for 5% of congenital malformations.[2], it represents the most frequent congenital abnormalities (5 to 10/1000) of malformations in the central nervous system. Every year a $NTD_s$ affects 250,000 pregnancies worldwide. The etiology of these abnormalities is complex involving environmental factors and genetic factors. Cephalic forms are distinguished as anencephaly, exencephaly**,** meningoencephalocele and spinal forms such as spinas bifidas. Anencephaly and spina bifidas are the most common neural tube abnormalities.

Oro-facial clefts represent one of the most common congenital malformations among children.[3] It occurs in an isolated or multiple way and results from an interaction between environmental and genetic factors.[4] It includes cleft palate (CP), cleft lip (CL) and cleft labio-palatal (CLP). Facial malformations are psychologically very cumbersome for the child (physical discomfort, such as difficulty in eating, breathing, hearing and speaking) and for his/her parents.

In order to prevent and reduce the prevalence of these congenital malformations, several countries in the world, notably Morocco, have adopted a policy in favor of periconceptional folic acid supplementation targeted at women of childbearing age and those at high risk of

adverse events of these malformations and as well the fortification of basic foodstuffs, in Morocco the flour is fortified with iron and folic acid. The aim of this study is to evaluate the effectiveness of this strategy and to produce objective data on the current situation of these birth defects in our country in order to enable decision-makers to take the necessary measures to improve their surveillance and accelerate their diagnosis and management.

**Patients and methods**

This prospective, multicenter, study was carried out over a period of 36 months (from January 2012 to December 2014) at 20 public hospitals in Morocco and covered the following regions:

Oued Eddahab-Lagouira, Laayoune-Boujdour-Sakia Lhamra, Guelmim-Smara, Souss-Massa-Darâa, El Gharb-Chrarda-Bni Hssen, Chaouia-Ouardigha, Marrakech-Tensift-El Haouz, Oriental, Grand Casablanca, Rabat-Salé-Zemmour-Zaër, Doukkala-Abda, Tadla-Azilal, Meknes-Tafilalet, Fes-Boulemane, Taza-Al Hoceima-Taounate and finally Tangier-Tetouan.

**Inclusion criteria**

We included in this study all live births, born in one of the medical structures concerned during the study period and having at least one abnormality of closure of the clinically visible neural tube isolated or associated with a congenital malformation as well as the oro-facial clefts.

- $TND_s$ were divided into two groups: 1) the spina bifida group including open spinal dysraphism (meningocele, myelomeningocele) and spina bifida occulta; 2) the anencephaly group defined by the absence of a cranial vault with total or partial absence of the brain.
- The oro-facial clefts are divided into three groups: 1) cleft palates, 2) clefts lip and 3) cleft labiopalatal

**Exclusion criteria**

We excluded from the study live births with no neural tube defects closure and oro-facial clefts, fetal deaths in utero (FDIU) after 22 weeks of amenorrhea (WA) and Medical Interruption of Pregnancy.

**Sources of information**

The data come from the maternity hospitals of the 20 Moroccan hospitals in the study. Notification registers have been set up for this purpose, with a predefined circuit, training of the healthcare providers who provide the notification and a monthly transfer of the data thus compiled to The Nutrition Cell of the Population Department of the Ministry of Health which makes the treatment.

**Data collection**

We used an active method for data collection. The information was collected on a daily basis using a computerized form specifying the following data: (a) the residence environment, (b) the type of neural tube defects, (c) the nature of the Oro-facial clefts, (d) the fate of cases of malformations.

**Definitions of Terms**

***spina bifida***

This is a bone segmental malformation of the rachis characterized by an opening of the posterior neural arch. They affect the meningeal envelopes, the spinal cord and the roots to a different degree. It is accompanied or not by hydrocephalus.

***Anencephaly***

This is a malformation of the neural tube characterized by a lack of closing of the cranial part of the nevrax, leading to the absence of development of the cranial vault, the meninges, the scalp with a little or no brain tissue. This malformation is incompatible with life.

***Cleft palate*** it is the absence of welding of the palate that can interest only the veil but also partially or totally the whole palate.

***Cleft lip*** is an absence of fusion of the embryonic tissue of the face or facial mesenchyme leading to a loss of substance of the upper lip.

***Cleft* labio-palatal** or clefts of the primary and secondary palate: it is a kind of notch that reaches the lip, the alveolar process, the hard palate (bone) and the soft palate (veil).

**Statistical analysis**

The analysis of the data and the calculation of malformations rates are carried out using the statistical software SPSS version 17.0 and Microsoft Excel. The comparison of the

distributions was carried out using the Chi2 test or Fisher's exact test, with a significance value of p <0.05.

## RESULTS

### 1. Annual and regional births' data

- ***Number of births***

This prospective study covered the period of 2012-2014, during which 819224 births were identified. The annual change in births (Figure 1) highlighted a non-significant decrease in the total number of births and the number of live births during the year of 2013 (Spearman correlation coefficient r = -0.50, p = 0.667).

The 819224 are divided up into 774 538 (94.55%) live births and 44 686 (5.45%) stillbirths.

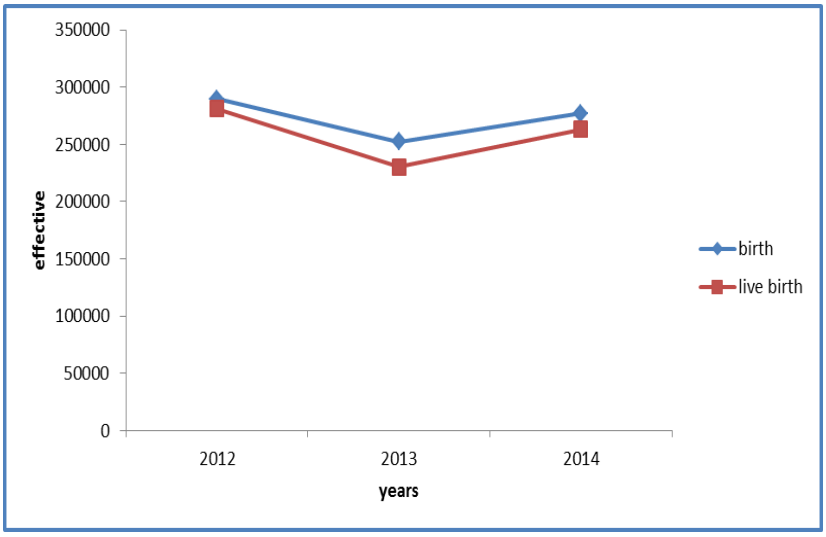



**Figure 1: Trends in live births and births in maternity hospitals in 20 public hospitals (Morocco 2012-2014).**

- ***Regional distribution of births***

The regional distribution of births was marked by an unequal distribution of live births (Figure 2). Thus, the average number of live births recorded during the study period is 48409.31 (95% CI: 34967.65-61860.53) with extremes of 892 (Oued Eddahab-Lagouira region) and 108325 (Marrakech-Tensift-El Haouz region).

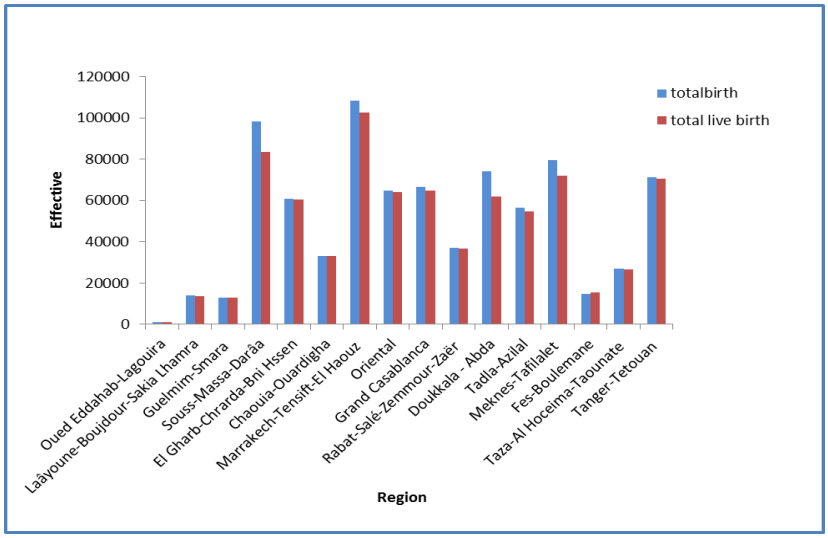
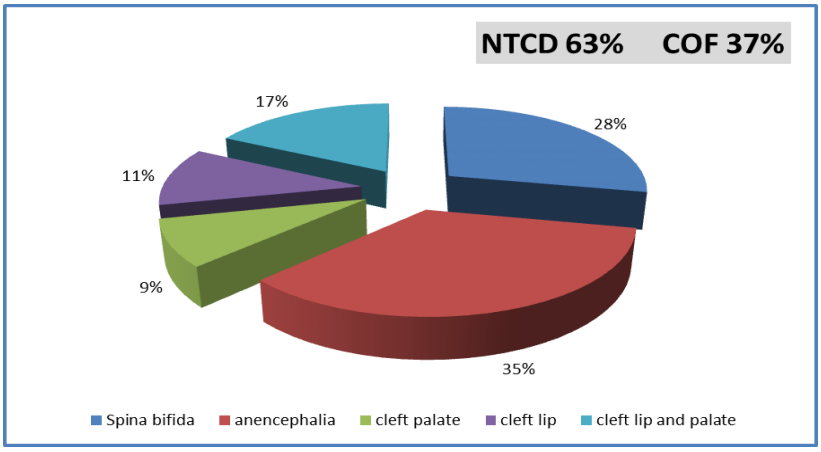



**Figure 2: Regional distribution of births and live births in maternity hospitals in 20 public hospitals (Morocco 2012-2014)**

## 2. Prevalence of Neural Tube Closure defects and Oro-Facial clefts

Five hundred and twenty six (526) malformations were collected in the period of 2012-2014 divided into 330 (62.74%) cases of anomalies of neural tube closures and 196 (37.26%) cases of oro-facial clefts, which represents a prevalence of 4.30 and 2.50 respectively, for 10.000 live births. The total prevalence of all the malformed is 6.79 per 10,000 live births. Figure 3 shows the distribution of these 526 anomalies. The Neural Tube Closure defects represent the most predominant anomalies in our study in which the most frequent malformations were anencephaly for Neural Tube Closure defects (Table 1) and clefts lip and palate for orofacial clefts (Table 2).




*NTC D: neural tude closure defect, COF: oro-facial cleft.*

**Figure 3: Breakdown of Neural Tube Closure Anomaly and Oro-Facial Splits in the Period 2012-2014**

**Table 1: Number of recorded cases of neural tube closure defects in the maternity wards of the 20 public hospitals (Morocco, 2012-2014)**

| Neural tube defects | Number of cases | Rate of NTCD* |
|---|---|---|
| Spina bifida | 148 | 1.91 |
| anencephalia | 182 | 2.35 |
| Total | 330 | 4.26 |

**Per 10,000 live births, ACNT: anomalies of closure of the neural tube.*

**Table 2: Number of recorded cases of oro-facial clefts in the maternity wards of the 20 public hospitals (Morocco, 2012-2014)**

| Oro-facial clefts | Number of cases | Rate of OFC* |
|---|---|---|
| Cleft palate | 46 | 0.59 |
| Cleft lip | 58 | 0.75 |
| Cleft labio-palatal | 92 | 1.19 |
| Total | 196 | 2.53 |

**Per 10,000 live births, OFC: Oro-facial clefts.*

### 3. Annual evolution of neural tube closure defects and oro-facial clefts

Figure 4 shows the evolution of all the observed anomalies showing a significant decrease in the total number of malformed persons between 2012 and 2014 (Spearman coefficient r = -1, p = 0.01). The average number of the malformed is 175 with extremes of 230 in 2012 and 135 in 2014. The total malformed rate increased from 8.18 to 4.80 per 10,000 live births during the period of 2012-2014. The analysis of rates' evolution (per 1000 births) of malformations recorded annually of neural tube and oro-facial clefts (Figure 5) revealed a significant decrease in rates of spina bifida, anencephaly, palate clefts, labial clefts and Labio-palatam clefts (p = 0.01). The analysis of the overall data also revealed a significant decrease in the prevalence of neural tube closure anomalies and oro-facial clefts during the period of 2012-2014. Indeed, annual anomalies of neural tube closures rates and oro-facial clefts decreased respectively from 5.05 to 3.5 / 10,000 and 3.13 to 1.64 / 10,000 live births, which was statistically significant (p = 0.01).

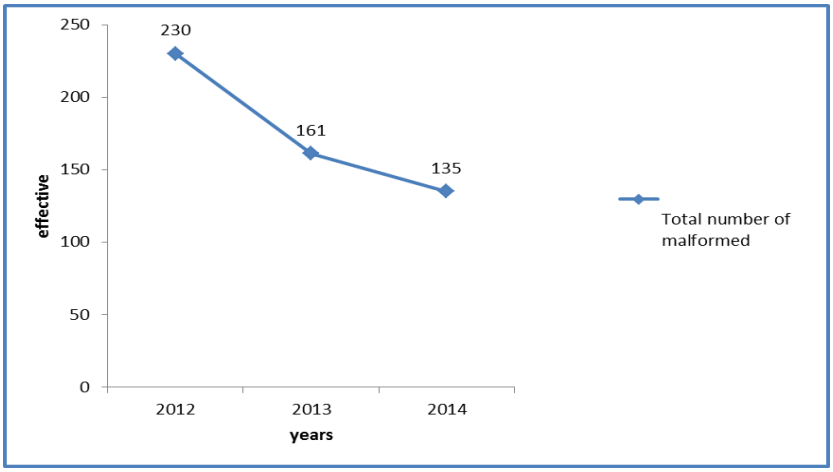



**Figure 4: trend in the total malformations recorded annually in the maternity wards of the 20 public hospitals in Morocco during the period 2012-2014.**

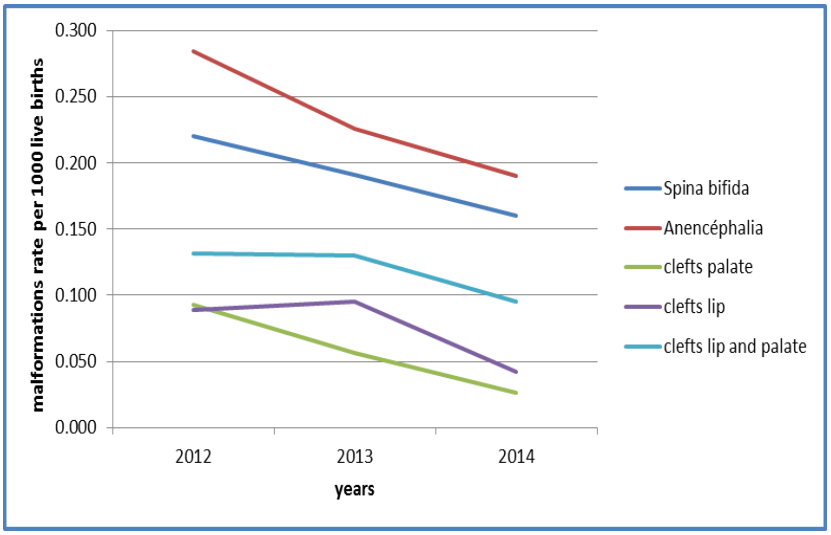



**Figure 5: Rate (per 1,000 live births) of each congenital malformation recorded annually in the maternity hospitals of the 20 public hospitals in Morocco during the period 2012-2014**

### 4. Regional distribution of neural tube closure defects and oro-facial clefts

Concerning the comparative situation of the regions for the whole anomalies of neural tube closures and the oro-facial clefts analysis of the overall results reveals an unequal distribution of these anomalies. The highest rates affect the regions: Oued Eddahab-Lagouira (11.21 per 10,000 live births), Laâyoune-Boujdour-SakiaLhamra (8.7 per 10,000 live births) Doukkala - Abda (7.9 for 10 (3.86 per 100,000 live births), for the anomalies of neural tube closures and the regions, Guelmim-Smara (3.86 per 10,000 live births), Marrakesh-Tensift-El Haouz (3.90 per 10,000 live births), Grand Casablanca Living), Rabat-Salé-Zemmour-Zaër (4.90 per 10,000 live births) for oro-facial clefts.

Moreover, the distribution by type of neural tube closure anomalies and oro-facial clefts differs from a region to another. An analysis of the results of the regional rates of neural tube diseases (Table 3) and of the oro-facial clefts (Table 4) revealed a regional disparity in these deformities. The highest regional rates affect the regions of Oued Eddahab-Lagouira (11.2 per 10,000 live births) and Doukkala-Abda (5.65 per 10,000 live births) for Spina bifida, the Laayoune-Boujdour-Sakia Lhamra regions (7.25 per 10,000 live births) and Taza-Al Hoceima- Taounate (6.37 per 10,000 live births) for anencephaly, the Laayoune-Boujdour-Sakia Lhamra regions (2.18 per 10,000 live births) and Guelmim-Smara (2.31 per 10,000 live births) for the palate cleft, the Marrakech-Tensift region -El Haouz (1.46 per 10,000 live births) for the labial clefts and (2.44 per 10,000 live births) for the labio-palatal clefts.

Furthermore, Table 5 shows the distribution of all the malformations in the different regions of Morocco. There was a statistically significant difference in the regional percentages of neural tube closure defects and oro-facial clefts (chi-square, $p<0.001$).

**Table 3: Regional rates of neural tube closure defects in the maternity wards of the 20 public hospitals (Morocco, 2012-2014)**

| Region | Spina bifida[a] | Rate of Spina bifida[b] | anencéphalia[a] | Rate of anencéphalia[b] |
|---|---|---|---|---|
| Oued Eddahab-Lagouira | 1 | 11.21 | 0 | 0 |
| Laâyoune-Boujdour-Sakia Lhamra | 2 | 1.45 | 10 | 7.25 |
| Guelmim-Smara | 0 | 0.00 | 2 | 1.54 |
| Souss-Massa-Darâa | 5 | 0.60 | 11 | 1.32 |
| El Gharb-Chrarda-Bni Hssen | 14 | 2.31 | 30 | 4.95 |
| Chaouia-Ouardigha | 2 | 0.61 | 2 | 0.61 |
| Marrakech-Tensift-El Haouz | 22 | 2.14 | 19 | 1.85 |
| Oriental | 10 | 1.56 | 9 | 1.40 |
| Grand Casablanca | 9 | 1.39 | 8 | 1.23 |
| Rabat-Salé-Zemmour-Zaër | 4 | 1.09 | 11 | 3.00 |
| Doukkala - Abda | 35 | 5.65 | 14 | 2.26 |
| Tadla-Azilal | 16 | 2.93 | 15 | 2.74 |
| Meknes-Tafilalet | 14 | 1.94 | 16 | 2.22 |
| Fès-Boulemane | 3 | 1.94 | 3 | 1.94 |
| Taza-Al Hoceima-Taounate | 4 | 1.50 | 17 | 6.37 |
| Tanger-Tetouan | 7 | 0.99 | 15 | 2.13 |
| total | 148 | 1.91 | 182 | 2,35 |

*[a]number of cases , [b]Rate per10 000 live birth.*

**Table 4: Regional rates of oro facial clefts ts in the maternity wards of the 20 public hospitals (Morocco, 2012-2014)**

| Region | Cleft palate[a] | Rate[b] | Cleft lip[a] | Rate[b] | Cleft lip and palate[a] | Rate[b] |
|---|---|---|---|---|---|---|
| Oued Eddahab-Lagouira | 0 | 0 | 0 | 0 | 0 | 0 |
| Laâyoune-Boujdour-Sakia Lhamra | 3 | 2.18 | 0 | 0 | 1 | 0.73 |
| Guelmim-Smara | 3 | 2.31 | 1 | 0.77 | 1 | 0.77 |
| Souss-Massa-Darâa | 3 | 0.36 | 4 | 0.48 | 3 | 0.36 |
| El Gharb-Chrarda-Bni Hssen | 7 | 1.16 | 2 | 0.33 | 1 | 0.17 |
| Chaouia-Ouardigha | 0 | 0.00 | 0 | 0.00 | 1 | 0.30 |
| Marrakech-Tensift-El Haouz | 0 | 0.00 | 15 | 1.46 | 25 | 2.44 |
| Oriental | 2 | 0.31 | 3 | 0.47 | 9 | 1.40 |
| Grand Casablanca | 10 | 1.54 | 5 | 0.77 | 9 | 1.39 |
| Rabat-Salé-Zemmour-Zaër | 6 | 1.63 | 4 | 1.09 | 8 | 2.18 |
| Doukkala - Abda | 3 | 0.48 | 7 | 1.13 | 7 | 1.13 |
| Tadla-Azilal | 1 | 0.18 | 6 | 1.10 | 2 | 0.37 |
| Meknes-Tafilalet | 2 | 0.28 | 6 | 0.83 | 7 | 0.97 |
| Fes-Boulemane | 1 | 0.65 | 1 | 0.65 | 3 | 1.94 |
| Taza-Al Hoceima-Taounate | 0 | 0.00 | 2 | 0.75 | 6 | 2.25 |
| Tanger-Tetouan | 5 | 0.71 | 2 | 0.28 | 9 | 1.28 |
| Total | 46 | 0.59 | 58 | 0.75 | 92 | 1,19 |

[a]*number of cases , Rate per 10 000 live birth.*

**Table 5: Percentage of neural tube closure defects and oro-facial cleftsts in the maternity wards of the 20 public hospitals in different regions of Morocco during the period 2012-2014**

| Region | Malformation N=526 | | | | | *p* |
|---|---|---|---|---|---|---|
| | Spina bifida n(%) | Anencé-phalie n(%) | Cleft palate n(%) | Cleft lip n(%) | Cleft lip and palate n(%) | |
| Oued Eddahab-Lagouira | 1(0.7) | 0(0) | 0(0) | 0(0) | 0(0) | <0.001 |
| Laâyoune-Boujdour-Sakia Lhamra | 2(1.4) | 10(5.5) | 3(6.5) | 0(0) | 1(1.1) | |
| Guelmim-Smara | 0(0) | 2(1.1) | 3(6.5) | 1(1.7) | 1(1.1) | |
| Souss-Massa-Darâa | 5(3.4) | 11(6) | 3(6.5) | 4(6.9) | 3(3.3) | |
| El Gharb-Chrarda-Bni Hssen | 14(9.5) | 30(16.5) | 7(15.2) | 2(3.4) | 1(1.1) | |
| Chaouia-Ouardigha | 2(1.4) | 2(1.1) | 0(0) | 0(0) | 1(1.1) | |
| Marrakech-Tensift-El Haouz | 22(14.9) | 19(10.4) | 0(0) | 15(25.9) | 25(27.2) | |
| Oriental | 10(6.8) | 9(4.9) | 2(4.3) | 3(5.2) | 9(9.8) | |
| Grand Casablanca | 9(6.1) | 8(4.4) | 10(21.7) | 5(8.6) | 9(9.8) | |
| Rabat-Salé-Zemmour-Zaër | 4(2.7) | 11(6) | 6(13) | 4(6.9) | 8(8.7) | |
| Doukkala - Abda | 35(23.6) | 14(7.7) | 3(6.5) | 7(12.1) | 7(7.6) | |
| Tadla-Azilal | 16(10.8) | 15(8.2) | 1(2.2) | 6(10.3) | 2(2.2) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Meknes-Tafilalet | 14(9.5) | 16(8.8) | 2(4.3) | 6(10.3) | 7(7.6) | |
| Fes-Boulemane | 3(2) | 3(1.6) | 1(2.2) | 1(1.7) | 3(3.3) | |
| Taza-Al Hoceima-Taounate | 4(2.7) | 17(9.3) | 0(0) | 2(3.4) | 6(6.5) | |
| Tanger-Tetouan | 7(4.7) | 15(8.2) | 5(10.9) | 2(3.4) | 9(9.8) | |

*Values are expressed in count and percentage.*

### 5. Becoming neural tube closure defects and oro-facial clefts

One hundred and seventy-eight deaths were recorded among 526 malformations, for a prevalence of 33.84%. The analysis in Table 6 highlighted an unequal regional distribution of mortality. Thus, the average percentage of deaths by anomalies of neural tube closures and oro-facial clefts is 40.51% with extremes of 0% (OuedEddahab-Lagouira region) and 100% (Chaouia-Ouardigha region).

**Table 6: Regional distribution of deaths by neural tube closure defects and oro-facial clefts in the maternity wards of 20 public hospitals (Morocco, 2012-2014)**

| Region | Number of cases* | Number of deaths | Percentage% |
|---|---|---|---|
| Oued Eddahab-Lagouira | 1 | 0 | 0 |
| Laâyoune-Boujdour-Sakia Lhamra | 16 | 11 | 68.75 |
| Guelmim-Smara | 7 | 3 | 42.86 |
| Souss-Massa-Darâa | 26 | 3 | 11.54 |
| El Gharb-Chrarda-Bni Hssen | 54 | 9 | 16.67 |
| Chaouia-Ouardigha | 5 | 5 | 100.00 |
| Marrakech-Tensift-El Haouz | 81 | 17 | 20.99 |
| Oriental | 33 | 4 | 12.12 |
| Grand Casablanca | 41 | 20 | 48.78 |
| Rabat-Salé-Zemmour-Zaër | 33 | 18 | 54.55 |
| Doukkala - Abda | 66 | 21 | 31.82 |
| Tadla-Azilal | 40 | 12 | 30.00 |
| Meknes-Tafilalet | 45 | 12 | 26.67 |
| Fes-Boulemane | 11 | 10 | 90.91 |
| Taza-Al Hoceima-Taounate | 29 | 7 | 24.14 |
| Tanger-Tetouan | 38 | 26 | 68.42 |

** total number of neural tube deseases and oro-facial clefts.*

## DISCUSSION

The present study allowed analyzing prospectively the rates of neural tube closure defects and facial malformations in 20 public hospitals in different regions of Morocco. It was carried out over a period of 36 months and concerned 774538 live births that is to say 94.55% of births. These embryopathies were chosen because of their importance as a cause of neonatal mortality, chronic morbidity and child disability in many industrialised

countries.[5,6,7,8] In our study, Five hundred and twenty six malformed birds were recorded, an overall prevalence of 6.79 per 10,000 live births. The notified anomalies of neural tube closures cases concerned only spina bifida and anencephaly. The notified cases of the oro-facial clefts only concerned the CP, CL and CLP.

Anomalies of neural tube closures were the most frequent abnormalities in this study, accounting for 62.74% (330/526) of all anomalies. In literature, these abnormalities account for most of the malformations of the central nervous system.[9] The prevalence per 10,000 live births of each type of $NTD_s$ was evaluated during the study period. The results gave a total prevalence of 4.26 per 10,000 live births (Table 1). In France, the prevalence of anomalies of closure of the neural tube, in particular spina bifida and anencephaly, affects nearly 1 birth per thousand live births and medical terminations of pregnancy.[10] In India the prevalence of this type of malformation varies from 0.06 to 1.3 per 10,000 births and in a national study similar to that we conducted the prevalence was 0.12 per 10,000 births.[2]

For the anomalies of the oro-facial clefts, the prevalence of all clefts in our study is 2.53 per 10,000 live births (Table 1), by around 1 case per 4,000 live births. The proportion of oro-facial clefts is 37% among all malformed patients during the period 2012-2014. The prevalence of these abnormalities in our study appears to be lower than that reported in the literature because we excluded stillbirths from the study, fetal deaths in utero after 22 SA and Medical Interruption of Pregnancy which represent a non-negligible proportion of congenital malformations.

The frequency of each type of $NTD_s$ at birth was assessed during the period 2012-2014. The results gave a spina bifida frequency of 1.91 per 10,0000 live births that of anencephaly of 2.35 per 10,000 live births. Our study highlights a similar prevalence of these abnormalities. CLP were the most frequent anomalies among oro-facial clefts, that is, approximately 0.2 per 1,000 live births against 0.06 for CL and 0.07 for CP (Table 2).

At the same time, the analysis of the evolution of all congenital malformations in general, and the anomalies of neural tube closures in particular (Figures 4 and 5) revealed a statistically significant decrease in malformed rates from 8.18 to 4.80 and 5.05 to 3.50 per 10,000 live births during the period 2012-2014. This interesting point in our study highlights the effectiveness of Morocco's strategy since 2007 concerning the folic acid supplementation of women during the periconceptional period as part of the prevention of $NTD_s$. Indeed, the

efficacy of folic acid in primary and secondary prevention of neural tube defects has been demonstrated by randomized controlled trials[11] and by numerous studies which have demonstrated a relationship between the occurrence of this type of malformations and a Folic acid deficiency in the case of a history as well as in the absence of identified risk factors In Sweden, the consumption of folic acid in the conceptional period is a national strategy and has significantly reduced the prevalence of neural tube defects.[12] The results of these studies led several countries to define a prevention policy aimed at increasing the intake of folic acid in women before the onset of pregnancy. These policies were introduced in the United Kingdom in 1992, in the Republic of Ireland in 1993, and in the Low Netherlands in 1993.

In France, recommendations were made by the societies of pediatrics in 1995 and of obstetrics in 1997[13], In 2000, the Directorate-General for Health issued recommendations for the prevention of $NTD_s$ to health professionals, whom were as well charged To take care of all women of reproductive age. The recommendations focused on increasing the level of folate by only changing dietary habits (consumption of folate-rich foods), or in combination at the time of supplementation as part of planning for a pregnancy.[14,15] In a few countries, including the United States, in order to ensure a sufficient daily dietary intake of folic acid, a fortification of basic foodstuffs was put in place by the Center for Disease Control in Atlanta starting from 1998,which was in addition to recommendations for folic acid supplementation. The effectiveness of this program was evaluated by a study conducted in the United States which reported a 31% reduction in risk following the mandatory introduction of enrichment measures for all US-grown flours and cereals.[16]

in order to prevent and reduce the prevalence of these TNDs In Morocco, a policy of fortification of flour was adopted in 2006 and in 2007 the national nutrition program, notably in the framework of the strategy that aims to combat micronutrient deficiencies, established a system for reporting neural tube defects in relation to folic acid deficiency, this system made it possible to make an inventory of the situation, to have national data of these malformations and to evaluate the effectiveness of the interventions undertaken such as the fortification of flour and the supplementation in folic acid of the women at risk during the periconceptional period.[17] Our work confirmed the effective action of this policy adopted in Morocco in order to reduce the incidence of these pathologies. Indeed, our results have highlighted a significant decrease in TNDs from 5.05 per 10,000 live births to 3.50 per 10,000 live births during the period 2012 - 2014.

Moreover, a significant regional disparity ($p<0.001$) was observed in our study for all malformed patients and according to the type of malformation.

The most affected areas were: the Oued Eddahab-Lagouira region (11.2 per 10,000 live births) for Spina bifida, the Laayoune-Boujdour-Sakia Lhamra regions (7.25 per 10,000 live births) and Taza-Al Hoceima-Taounate 6.37 per 10,000 live births) for anencephaly, the Guelmim-Smara region (2.31 per 10,000 live births) for cleft palate and the Marrakech-Tensift-El Haouz region for cleft lip (1.46 per 10,000 live births) and the labio-palatal clefts (2.44 per 10,000 live births, Table 3 and 4). Our results are consistent with data from the literature that reported significant variations in some regions. Indeed, if TNDs are among the most frequent congenital malformations, their prevalence varies according to the geographic region, the sex of the child reached and the geographic origin of the parents.[18] The frequency of spina Bifidas is subject to secular and geographical variations. In France, it was estimated at 0.52 ‰ between 1965 and 1975, but the incidence is higher in certain regions (northern Finistère: 2.7 ‰). Worldwide, the highest frequencies were observed in Scotland, Ireland and Wales, where they were 5-6 ‰. In Morocco in Casablanca, the census of the Department of Neurosurgery at Ibn Rochd Hospital is an average of 12 cases per year of spina bifida between 1981 and 1993.[17]

In addition, the frequency of oro-facial clefts and their anatomical distribution vary according to geographical and ethnic origin.[19,20,21] The prevalence of oro-facial clefts in African women is 0.2 to 0.3 / 1000 whereas it is within 2 to 3/1000 among the Caucasians and 1/1000 in the Asians.[22] The distribution of these anomalies also varies according to sex[23], environmental factors such as tobacco, alcohol, ionizing radiation and maternal factors, particularly folate deficiency[24], But these factors did not form part of the subject of our work.

Concerning the fate of the malformed, 178/526 deaths were reported in this study, a prevalence of 33.83%, which corresponds to 1/3 of all cases of malformations. This important proportion can be explained by the high frequency of anencephaly in our population, which is an embryopathy incompatible with life. Generally a small percentage (30-33%) will live and survived for a few moments to a few days. Rare cases have lived for several months.

Most infants with anencephaly will always be born. A small percentage (30-33%) The analysis in Table 6 highlighted an uneven regional distribution of mortality. Thus, the average percentage of deaths by anomalies of neural tube closures and oro-facial clefts is 40.51% with extremes 0% (Oued Eddahab-Lagouira region) and 100% (Chaouia-Ouardigha region).

Our work has focused only on the prevalence and regional distribution of these congenital anomalies; which is a limit to the study since the risk factors were not sought. A broader study including all risk factors should be considered for specific prevention measures.

## CONCLUSION

This study made it possible on the one hand to make an inventory of the prevalence of neural tube closure defects and the oro-facial clefts in Morocco during the period 2012-2014 and on the other hand to evaluate The effectiveness of the national strategy in preventing these anomalies through the implementation of the fortification of basic folic acid foods and the management of women in the periconceptional period in general and women at risk in particular to reduce the prevalence of these embryopathies, which are still an important cause of neonatal mortality and morbidity in many countries of the world and especially in Morocco.

### State of current knowledge on the subject

- Neural tube closure anomalies and oro-facial malformations remain the most common congenital malformations among children. They are an important cause of neonatal mortality and morbidity in Morocco;
- Folic acid supplementation during the periconceptional period has contributed to the prevention of several congenital anomalies and more particularly the anomalies of neural tube closures.

### Contribution of our study to knowledge

**The present study allowed**

- To analyze prospectively the rates of anomalies of neural tube closure and facial malformations in 20 Moroccan public hospitals during the period 2012-2014;
- To have national data on malformations and evaluate the effectiveness of the interventions undertaken. However, Morocco's strategy for folic acid supplementation of

women in periconceptional period and fortification of products should be encouraged as part of the prevention of these congenital anomalies.

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**Conflicts of interest**

The authors do not declare any conflict of interest.

**Author's contributions**

All the authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

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