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Cumulative incidence of lethal congenital anomalies in Peru

Incidencia acumulada de anomalías fetales incompatibles con la vida en Perú

Alvaro Taype-Rondan[1], Jessica Hanae Zafra-Tanaka[2], Enrique Guevara-Ríos[3], Susana Chávez-Alvarado[4]

[1] Universidad San Ignacio de Loyola - Research Unit for the Generation and Synthesis of Health Evidence - Lima - Peru.
[2] Universidad Peruana Cayetano Heredia - CRONICAS Center of Excellence for Chronic Diseases - Lima - Peru.
[3] Instituto Nacional Materno Perinatal - Management - Lima - Peru.
[4] Centro de Promoción y Defensa de los Derechos Sexuales y Reproductivos - Management - Lima - Peru.
Correspondencia: Susana Chávez Alvarado. PROMSEX Centro de Promoción y Defensa de los Derechos Sexuales y Reproductivos. Avenida José Pardo 601, office: 604. Telephone number: +51 1 4478668, ext.: 114. Lima. Peru.
Email: susana@promdsr.org..

Abstract

Introduction: Lethal congenital anomalies (LCA) are anomalies associated with early stillbirth or newborn death. Currently, there are no data on the incidence of LCAs in Peru.
Objectives: To estimate the cumulative incidence of LCAs in Peru, the Department of Lima, and six hospitals located in the city of Lima (Peru), and to describe the characteristics of LCA cases reported between 2012 and 2016 at Instituto Nacional Materno Perinatal (INMP), located in Lima, Perú.
Materials and methods: Cumulative incidence of LCAs in Peru was determined based on the cases reported in a five-year period, which varied depending on data accessibility (2011-2015 and 2012-2016). In addition, the medical records of neonates with LCA registered at INMP were reviewed to identify the characteristics of these cases.
Results: Cumulative incidence of LCAs in Peru was 0.89 cases per 10 000 newborns, while at INMP it was 7.19 cases. Out of 48 newborns with LCAs treated at INMP during the study period, 54.2% were born with neonatal depression, and 83.3% died during their hospital stay.
Conclusion: Cumulative incidences of LCAs reported here (Lima, Department of Lima, and Peru) were lower than those described by international epidemiological surveillance systems, which might be caused due to shortcomings related to the registration of these cases in the health institutions and records analyzed here.
Keywords: Congenital Abnormalities; Perinatal Mortality; Fetal Mortality (MeSH).

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Resumen

Introducción. Las anomalías fetales incompatibles con la vida (AFIV) son aquellas que se asocian con la muerte temprana del feto o del recién nacido. En la actualidad, se desconoce la magnitud de este problema en Perú.
Objetivos. Estimar la incidencia acumulada de AFIV en Perú, en el departamento de Lima y en seis hospitales de la ciudad de Lima, y describir las características de este tipo de anomalías reportadas entre 2012 y 2016 en el Instituto Nacional Materno Perinatal (INMP) de Lima, Perú.
Materiales y métodos. Se determinó la incidencia acumulada de las AFIV reportadas en un período de cinco años en Perú, el cual varió dependiendo de la disponibilidad de los datos (2011-2015 y 2012-2016). Además, se revisaron las historias clínicas de los neonatos con AFIV registradas en el INMP para obtener sus características.
Resultados. La incidencia acumulada de AFIV en todo el Perú fue de 0.89 por cada 10 000 recién nacidos y en el INMP fue 7.19. De los 48 recién nacidos con AFIV atendidos en el INMP, 54.2% nacieron con depresión neonatal y 83.3% fallecieron en el hospital.
Conclusión. Las incidencias acumuladas de AFIV encontradas fueron menores a las reportadas por los sistemas internacionales de vigilancia epidemiológica, lo que podría deberse a falencias en su registro en las instituciones de salud y registros analizados.
Palabras clave: Anomalías congénitas; Mortalidad perinatal; Mortalidad fetal (DeCS).

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Introduction

According to the Sociedad Española de Ginecología y Obstetricia (Spanish Society of Gynecology and Obstetrics), lethal congenital anomalies (LCA) are "anomalies that are predictably/usually associated with the death of the fetus or newborn during the neonatal period."[1, p97] While most of these cases result in death before or immediately after birth, some children may live for days or even years.[2,3] Thus, studying the incidence of LCAs is highly relevant, considering that it may reveal possible teratogenic agents.[4]

Multiple epidemiological surveillance systems and other primary studies have assessed the incidence of LCAs, since many of them are compiled by the International Clearinghouse Centre for Birth Defects (ICBDSR), which includes information from 29 countries.[5] One of the largest and most organized surveillance systems is the European Surveillance of Congenital Anomalies (EUROCAT), which consists of 23 European countries that follow a standardized data collection methodology.[6]

In Latin America, most countries do not have surveillance systems for LCAs, but some studies have reported new cases of congenital anomalies.[7,8] The Latin American Collaborative Study of Congenital Malformations (ECLAMC) collects data from several sentinel hospitals in 7 South American countries (4 from Chile, 4 from Argentina, 4 from Brazil, 2 from Bolivia, 4 from Venezuela, 1 from Colombia and 1 from Peru), although they do not report incidences for each country.[9] The data reported for Peru are provided by the Hospital Nacional Edgardo Rebagliati Martins (HNERM), a Social Security (EsSalud) referral institution located in Lima that treats pregnant women who are employed or have a partner who is employed. The HNERM is a reference center since it attends the largest number of births in EsSalud.[10]

Estimates are that 945 children are born with LCAs in Peru each year;[11] however, few studies have delved into this figure: Velásquez-Hurtado *et al.*[12] evaluated the records of neonatal deaths in the provincial municipalities of Huánuco and Ucayali and reported 1 case of trisomy 18 among 11 441 births in 2011; del Aguila-del Aguila[13] reviewed the records of the neonatal service of EsSalud's Hospital III Iquitos and reported 4 cases of anencephaly among 2 982 births in 2014; finally, Mansilla-Gallegos[14] analyzed the records of neonates with chromosomopathies at the Cytogenetics Laboratory of the Hospital Nacional Edgardo Rebagliati Martins and reported 25 cases of trisomy 18 and 11 of trisomy 13 among 25 086 births in the period 2013-2015. These studies did not assess the characteristics of infants with LCAs.

The lack of information on the incidence of LCAs and their characteristics does not allow measuring their impact on the Peruvian context. Therefore, this study has 2 objectives: to estimate the cumulative incidence of infants with LCAs in 6 hospitals of Lima, in the department of Lima and throughout Peru over a 5-year period, and to describe the characteristics of the cases reported between 2012 and 2016 at the Instituto Nacional Materno Perinatal (INMP) of Lima. It should be clarified that the INMP was selected to make the specific characterization of the anomalies because it is the reference hospital of the Ministry of Health (MINSA) and the one that attends the largest number of births in the country.[15]

Materials and methods

Study design

A secondary data analysis was conducted to estimate the cumulative incidence of infants with LCAs in six hospitals of Lima, the department of Lima and throughout Peru. For its part, the INMP carried out a retrospective analysis of the medical records of neonates born with congenital anomalies to describe their characteristics.

Definition of LCA

According to SEGO, which proposes a list of 17 of anomalies (Table 1), LCAs are defined as conditions that, due to their severity, do not require evaluation by a clinical committee to determine its classification, since it would be considered as such anywhere in the world due to its poor prognosis.[1] However, since the records analyzed were based on the 10th revision of the International Classification of Diseases (ICD-10),[16] it was only possible to evaluate the 9 LCAs currently included in that classification. It should be noted that the term LCA has not yet been adopted by the Peruvian health system.

Table 1. List of lethal congenital anomalies according to the Sociedad Española de Ginecología y Obstetricia.

N	Diagnosis	ICD-10 Code	Evaluated in this study
1	Anencephaly/ Acephaly/Acrania	Q00.0	Yes
2	Holoprosencephaly	Q04.2	Yes
3	Renal agenesis, bilateral	Q60.1	Yes
4	Potter's syndrome	Q60.6	Yes
5	Thanatophoric short stature	Q77.1	Yes
6	Trisomy 18	Q91.0 - Q91.3	Yes
7	Trisomy 13	Q91.4 - Q91.7	Yes
8	Trisomy 9	Q92.0 - Q92.1	Yes
9	Triploidy and polyploidy	Q92.7	Yes
10	Hydranencephaly	-	No
11	Laryngeal atresia	-	No
12	Tracheal atresia	-	No
13	Agenesis of the diaphragm	-	No
14	Ectopia cordis	-	No
15	Pentalogy of Cantrell	-	No
16	Amniotic band syndrome	-	No
17	Limb-body wall complex	-	No

ICD-10: International Classification of Diseases, 10th revision.
Source: Elaboration based on the data of the Sociedad Española de Ginecología y Obstetricia [1] and the ICD-10.[16]

A newborn with LCA was that which had one of the 9 LCA diagnoses contemplated in the ICD-10. Anomalies that were not coded in the ICD-10 were not included in the study as it was not possible to identify them. Cumulative incidence was used as a unit of measurement; it was estimated by dividing the number of reported LCA cases by the number of live births in the period studied, which, for accessibility reasons, varied as follows: from 2011 to 2015 in the Hospital Nacional Arzobispo Loayza (HNAL), the Hospital Nacional Docente Madre Niño San Bartolomé (HONADOMANI) and the records from Peru and Lima, and from 2012 to 2016 in the Hospital Nacional Cayetano Heredia (HNCH), the Hospital María Auxiliadora (HMA), theHospital Nacional Sergio E. Bernales (HNSEB) and the INMP.

Procedures

Information on the incidence of the 9 LCAs contemplated in the ICD-10 was collected over a 5-year-period for all of Peru, the department of Lima, 5 hospitals in Lima and the INMP from three sources:

For all of Peru and for the department of Lima. This information was requested from the MINSA's Public Information Access System (SAIP),[15] which obtains its data from the hospital discharge records of the ministry's level II and III centers and merges them into the central statistics office. It should be noted that only the main diagnosis of each patient's epicrisis is found in these records. In addition, the total number of births reported to MINSA for all of Peru and the department of Lima was requested in order to calculate incidences.

For hospitals in Lima. This information was requested from the SAIP for each of MINSA's Level III hospitals in Lima, and only five responded: the HNCH, the HNAL, the HMA, the HONADOMANI and the HNSEB. Only the main diagnosis of the epicrisis of each newborn is found in these records. In addition, the number of births reported by each of the hospitals assessed was requested in order to calculate incidences.

For the INMP. The INMP's Statistics and Information Office was asked for the hospitalization databases of its neonatal service, in which the ICD-10 codes of each newborn born in that hospital were recorded, including stillborn children. After identifying the neonates with any of the 9 LCAs described in the ICD-10, a manual review of their medical records was performed to corroborate the diagnoses and extract the demographic and maternal/perinatal characteristics.

Variables

The main variable considered for the present study was the presence of any of the LCAs evaluated as described above. In the specific case of INMP, other variables collected during the review of medical records were: mother's age, gestational age at birth using the Capurro test (full term ≥37 weeks of gestation), type of delivery (vaginal or cesarean), neonatal depression (score <7 on the Apgar score 5 minutes after birth), sex of the newborn, hospitalization and death during the hospital stay.

Statistical analysis

Central tendency measures were used for the presentation of the results: dispersion for quantitative variables, and relative and absolute frequencies for qualitative variables. The analysis was done using Stata v14.0 (Stata Corp, College Station, TX, US).

Ethical considerations

This study followed the ethical principles outlined in the Declaration of Helsinki.[17] The research was based on secondary database analysis of, which were analyzed respecting privacy.

The protocol of the present study was approved by the INMP's Institutional Committee of Ethics through letter No. 0213-2017-DG-N°-083-OEAIDE/INMP of September 20, 2017.

Results

According to data provided by the SAIP for the periods studied (2011-2015 and 2012-2016), an incidence of 0.89 cases per 10 000 newborns was reported for Peru, 1.26 cases per 10 000 newborns for the department of Lima, and between 0.00 and 7.39 cases per 10 000 newborns for the 5 hospitals in the city of Lima from which data were obtained. Likewise, when evaluating INMP data, an incidence of 7.19 LCA cases per 10 000 newborns was obtained. The most frequent anomaly in this institution was anencephaly, followed by trisomy 18; no cases of bilateral renal agenesis, thanatophoric dysplasia, trisomy 9 or triploidy were reported (Table 2).

Sixty-six medical records of neonates with ICD-10 codes associated with some LCA were entered in the hospitalizations database of the INMP's neonatology service. However, a review of the medical records found that 18 had no diagnosis compatible with this type of anomalies, for a final count of 48 cases. After assessing the characteristics of the final sample, it was found that 20 infants died immediately after birth and the remaining 28 were hospitalized. In the end, 40 died in the hospital and no information was obtained on the survival of the remaining 8 once they were discharged (Table 3).

Discussion

The incidence of LCAs in Peru, the department of Lima, and 5 hospitals in Lima was established according to records provided by the SAIP, and the neonatal database of the INMP. The most frequent LCA was anencephaly, followed by trisomy 18. No cases of bilateral renal agenesis, thanatophoric dysplasia, trisomy 9 or triploidy were found.

Table 2. Incidence of lethal congenital anomalies per 10 000 births throughout Peru, in the department of Lima and six hospitals in the city of Lima.

Diagnosis	Peru * (2011-2015)	Department of Lima (2011-2015)	HNAL (2011-2015)	HONADOMANI (2011-2015)	HNCH (2012-2016)	HMA (2012-2016)	HNSEB (2012-2016)	INMP (2012-2016)
	n (Incidence)	n (Incidence)	n (Incidence)	n (Incidence)	n (Incidence)	n (Incidence)	n (Incidence)	n (Incidence)
Anencephaly/ Exencephaly/ Acrania	163 (0.71)	72 (1.02)	11 (5.42)	1 (0.29)	2 (0.91)	7 (1.81)	-	24 (3.59)
Trisomy 18	29 (0.13)	11 (0.16)	-	2 (0.59)	-	-	-	12 (1.80)
Alobar holoprosencephaly	-	-	1 (0.49)	1 (0.29)	-	1 (0.26)	-	6 (0.90)
Potter's syndrome	-	-	-	1 (0.29)	1 (0.46)	-	-	5 (0.75)
Trisomy 13	13 (0.06)	6 (0.08)	3 (1.48)	1 (0.29)	-	-	-	1 (0.15)
Bilateral renal agenesis	-	-	-	-	-	-	-	-
Thanatophoric dysplasia	-	-	-	-	-	-	-	-
Trisomy 9	-	-	-	-	-	-	-	-
Triploidy	-	-	-	-	-	-	-	-
Total	205 (0.89)	89 (1.26)	15 (7.39)	6 (1.76)	3 (1.37)	8 (2.07)	0 (0.00)	48 (7.19)
Newborns during the period	2 307 247	707 696	20 301	34 156	21 961	38 585	24 520	66 771

HNAL: Hospital Nacional Arzobispo Loayza; HONADOMANI: Hospital Nacional Docente Madre Niño San Bartolomé; HNCH: Hospital Nacional Cayetano Heredia; HMA: Hospital María Auxiliadora; HNSEB: Hospital Nacional Sergio E. Bernales; INMP: Instituto Nacional Materno Perinatal.
* Peru: figures for all of Peru.
Source: Own elaboration.

Table 3. Characteristics of neonates born with lethal congenital anomalies at the Instituto Nacional Materno Perinatal. 2012-2016.

Diagnosis	n	Mother's age	Gestational age at birth	Cesarean section delivery	Neonatal depression	Female sex	Hospitalized *	Immediate death after birth	Death during hospital stay
		$\bar{x}\pm\sigma$	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Anencephaly/ Exencephaly/ Acrania	24	29.2±7.1	13 (54.2)	8 (33.3)	18 (75.0)	8 (33.3)	9 (37.5)	15 (62.5)	24 (100.0)
Trisomy 18	12	32.1±8.0	3 (25.0)	7 (58.3)	3 (25.0)	5 (41.7)	11 (91.7)	1 (8.3)	9 (75.0)
Alobar holoprosencephaly	6	22.3±4.6	5 (83.3)	2 (33.3)	2 (33.3)	3 (50.0)	4 (66.7)	2 (33.3)	1 (16.7)
Potter's syndrome	5	25.8±7.2	2 (40.0)	3 (60.0)	2 (40.0)	3 (60.0)	4 (80.0)	1 (20.0)	5 (100.0)
Trisomy 13	1	23.0	0 (0.0)	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	1 (100.0)	1 (100.0)
TOTAL	48	28.6±7.5	23 (47.9)	20 (41.7)	26 (54.2)	20 (41.7)	28 (58.3)	20 (41.7)	40 (83.3)

$\bar{x}$: mean; σ: standard deviation.
Source: Own elaboration based on the data obtained in the study.

Cumulative incidence of LCAs

The incidence of LCAs found in the records for Peru, for the department of Lima and for most of the hospitals evaluated was lower than that found in the INMP database. This may be explained by differences in the methodology used, since INMP data were obtained from the hospital database, while central and hospital reports were used for the other populations evaluated (Peru, Lima department, and the other hospitals) and they only included the main diagnosis recorded in the patient's epicrisis at discharge, which may not necessarily be a LCA.

Other explanations to this difference in the incidence would be that other medical centers refer pregnant women with fetuses diagnosed with some LCA to the INMP, thus increasing its numbers. This could also be associated with the fact that the INMP, which has the largest neonatology service of the country, has trained personnel and the necessary supplies to make an adequate diagnosis of LCA, which would be underdiagnosed in other places.

On the other hand, the incidence for Peru (0.89 LCAs per 10 000 births) was much lower than that reported by international surveillance systems such as EUROCAT,[6] the Latin American Collaborative Study of Congenital Malformations (ECLAMC),[9] the National Registry of Congenital Anomalies of Argentina (RENAC)[18] and the Mexican Program for Registration and Epidemiological Surveillance of External Congenital Malformations (RYVEMCE),[19] which had incidents between 6.60 and 14.53. Since there is no reason to assume that the incidence of LCAs in Peru is lower than in other countries, estimates are that the records provided by the SAIP underestimate the figure by about 90%.

All this is very concerning, since knowing the actual magnitude of the problem, detect clusters of cases, carry out studies of associated factors and evaluate the impact of preventive measures, such as the use of folic acid supplements to avoid neural tube defects, is only possible if LCAs are properly reported.[20] This could be achieved by adopting an anomalies surveillance system as is the case of other countries and regions.[6,9,18,19]

Regarding international surveillance systems, the incidence reported by EUROCAT was twice as high as that reported by ECLAMC, RENAC, RYVEMCE and INMP. The reason may be that EUROCAT reports congenital anomalies in hospitals of various European countries in a standardized manner, while the other systems tend to combine hospitals and have varying degrees of standardization in their reporting. It is also possible that population differences, such as maternal age at conception and the spread of prenatal diagnosis in Europe, make EUROCAT records larger than those of other surveillance systems. Table 4 presents the incidents found by the above-mentioned international surveillance systems.

Table 4. Comparison between studies on incidences of lethal congenital anomalies per 10 000 births.

Diagnosis	Peru (2011-2015)	INMP (2012-2016)	RENAC (2012-2015)	EUROCAT (2011-2015)	ECLAMC (2007-2011)	RYVEMCE (2007-2011)
Anencephaly/Exencephaly/ Acrania	0.71	3.59	2.75	4.04	5.79	3.58
Trisomy 18	0.13	1.80	1.13	5.67	1.32	0.67
Alobar holoprosencephaly	-	0.90	2.38	1.51	0.78	1.79
Potter's syndrome	-	0.75	-	1.22	-	-
Trisomy 13	0.06	0.15	0.40	2.09	0.57	0.56
Bilateral renal agenesis	-	-	0.43	-	-	-
Thanatophoric dysplasia	-	-	0.12	-	-	-
Trisomy 9	-	-	-	-	-	-
Triploidy	-	-	-	-	-	-
Total	0.89	7.19	7.21	14.53	8.46	6.60

INMP: Instituto Nacional Materno Perinatal; RENAC: National Registry of Congenital Anomalies of Argentina; EUROCAT: European Surveillance of Congenital Anomalies; ECLAMC: Latin American Collaborative Study of Congenital Malformations; RYVEMCE: Mexican Program for Registration and Epidemiological Surveillance of External Congenital Malformations. Source: Own elaboration.

Characteristics of newborns with LCA

When reviewing the medical records of infants with LCAs born at INMP, it was found that 4 out of 10 died before they could be hospitalized, either in the delivery room or in the newborn's immediate care area, and that a similar proportion died during hospitalization. It should be noted that this high mortality is to be expected for this type of anomalies

When the different types of LCAs are studied separately, it can be seen that survival at discharge is almost entirely attributable to cases of holoproscencephaly and trisomy 18. Previous studies have also found a high survival rate related to these pathologies in the first week (71% and 65%, respectively), which drops drastically after the first year (47% and 16%, respectively).[2] This relatively long survival could impact the mother and the rest of her family financially and mentally, and this should be evaluated in future studies.

Implications

Most newborns with LCAs die, and if they survive, the degree of disability is high. Although these types of anomalies are rare, they are highly relevant because of their potential impact on mothers' physical and mental

health, such as psychological reactions of hopelessness, sadness, or guilt.[21-23] The magnitude of these damages has not been adequately assessed in countries where termination of pregnancy due to LCAs is illegal, and more studies are needed in Peru to assess the consequences and effectiveness of preventive interventions —such as the use of folic acid supplements for the prevention of anencephaly[24] or appropriate counseling on the mother's age at conception as a risk factor for trisomy 13 or trisomy 18—[25] and recovery interventions —including psychological support to the woman during and after pregnancy and avoiding medical futility in these babies.

Limitations and strengths

The main limitation of this study was the use of a secondary database (SAIP) and clinical records for the collection of information, which prevents ensuring that all diagnoses are reported, or that all the reported diagnoses are entered into the databases of the centers from which the information was obtained. Furthermore, since these databases only included the LCAs covered by the ICD-10,[16] it was not possible to track the 17 LCAs proposed by SEGO;[1] therefore, the cumulative incidence of LCAs is expected to be underestimated.

Another limitation is that the SAIP may have duplicate data, i.e. some patients may have gone to more than one hospital. However, due to the high lethality of LCAs during hospitalization and the underreporting observed, this was considered unlikely.

This is the first study that describes the incidence and characteristics of LCAs in Peru, so it is a relevant source of information to understand the impact and consequences that these anomalies can have in the country.

Conclusion

Cases of LCAs were reported for Peru, the department of Lima and six hospitals in Lima. The most frequent LCA was anencephaly, followed by trisomy 18, while no cases of bilateral renal agenesis, thanatophoric dysplasia, trisomy 9 or triploidy were found. In general, the incidences of LCAs found in this study are lower than those reported by international surveillance systems, which may be explained by shortcomings in the reporting of medical centers and the records analyzed.

Conflicts of interest

None stated by the authors.

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