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Comparative study of growth and morbid incidence among a group of infants born to mother with tuberculosis and a control group

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Estudio comparativo del desarrollo pondoestatural e incidencia mórbida entre un grupo de lactantes hijos de tuberculosa y otro de control.

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Introduction:

Tuberculosis (TB) or "white plague" was responsible for a great number of morbidity and mortality in industrialized societies of the nineteenth and early twentieth centuries. In the 1940s, the first articles about the efficacy of streptomycin for the treatment of TB in humans were published, which it was quickly known in our country, with surprising results[1]. Until that moment, most of the measures in order to control the disease were mainly preventive, recommending a complete isolation of the patients in sanatoriums, as well as the pasteurization of the dairy products and later, the immunization. The BCG vaccine, started to be used in the 1920s, was affected wiht the Lübeck disaster, in which 72 children died due to the administration of a BCG vaccine contaminated with a virulent bacillus, it was subjected to further investigations and reintroduced in 1947[2].

In the sanatorium era, patients were generally isolated and provided with a "*dietetic-hygienic*" cure[3], but given the high rates of infection in children and their dramatic evolution, it was recommended to separate the youngest from the family. "*Tuberculosis is contagious and if the child is in contact with his or her tuberculous parents, or in a tuberculous environment, it would be fatally tuberculous*"[4]. The school children were sent to preventoriums, in which there were also a series of measures in order to enhance their health, as receiving adequate food, rest, pure air, sun and exercise[5], while infants and young infants were admitted to foster care.

Thanks to these preventive measures, a slight decrease in the TB mortality rate was achieved, which some rates, like 260/100,000 inhabitants between 1903 and 1940 decreased to 196/100,000 between 1948 and 1949. These numbers re-

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presented a large gap with respect to reports from developed countries, such USA, in which rates had fallen to 50/100,000 inhabitants in the same period[6,7]. The poverty, overcrowding and poor hygienic conditions in which the national population was found did not contribute to national health indicators.

At the end of the 1940s, Chile was under a period of "*maximum tuberculosis*." In the analysis of 3009 autopsies performed on children between 0 and 16 years old, at the Manuel Arriaran Children's Hospital between 1943 and 1949, Dr. Julio Espinoza described that a 15% of the autopsied corpses were infected and/or died by TB; This positive rates of autopsies were lower in infants than in children older than 2 years old[8].

During that same period, Drs. Oscar Correa and Teodoro Zenteno followed a cohort of young infants hospitalized at Luis Calvo Mackenna Hospital for a period of at least 6 months. We reproduced part of the article, which stands out because it is one of the first cohorts published in our journal. Authors compared a cohort of 83 infants born to bacillary mothers and 76 children of healthy mothers hospitalized for social causes. They conclude that there is no difference in the incidence of infectious disease or in the growth between both groups. However, when comparing the tables with the current reference standards[9], we could notice the serious nutritional commitment of institutionalized infants, 75 years ago.

Dr. Oscar Correa and Dr. Teodoro Zenteno Article (published in 1948)

Introduction

The child of a tuberculosis mother has been the subject of long study for a long time. In this field, the doctors attention has been particularly drawn to the analysis along with the possibilities of bacillary contagion, development characteristics and the evolution of the disease in this type of infant.

A study as mentioned before requires, not only a voluminous material, but also a careful comparison of all the peculiarities during the evolution of the disease with those of a group of children whose mothers are healthy. To the above, it should be added that if valid results of this analysis are expected, study groups should be as closely homologous in conditions as medical and nursing and food care. It is not important to point out that no institution makes a better fulfillment of all these requirements. To be in charge of Infant Service for many years is a fortunate circumstance of Luis Calvo Mackenna Hospital, in which children, mostly healthy, remain interned a long time, due to social causes. This fact has encouraged us to perform the study, whose plan and results are discussed below.

Our purpose was to make a comparative analysis of the growth and morbid incidence among infants whose mothers had pulmonary tuberculosis and also among those who their mothers were healthy. In order to satisfy the first of these purposes, we decided to include in the study only infants in control from an early age, from the third month of life, which enabled to eliminate children with chronic nutritional damage.

The present work comprehend infants attended at Luis Calvo Mackenna Hospital, who were admitted in the establishment before their 3rd month of life and whose stay under the institutional care was extended from six months to at least two years. Given these requirements, the number of cases selected for analysis was only a fraction of the total number of infants admitted to the Service previously named. Thus, from 600 children registered from 1943 to mid-1948, only 159 were selected for this study.

We would like to know as accurately as possible all the characteristics of the evolution of a tuberculous child. To this effect, we grouped those selected children who were separated from their mothers with those who remained with their mothers at the moment of birth. It is worth highlighting that all the components of the disease came from the group who remained in the Maternity home, concluding that the indication of separation is successful. As for those children forming the group of those who made 'contact', most of whom were born in their own home and only a small number in Maternities, the separation method could not be effected, as occurred in the first case. If the separation was done, it was not possible to prolong it because there was no vacancy in the institution dedicated to this topic, which occurred in the latter.

The material include a total of 159 children, of whom in 76 there was no history of maternal tuberculosis, and in 83 cases, this data was positive. From 83 children, the separation method was performed in 57 of them, but in the remaining 26 was not possible. The material is composed of term infants, with an exception of 10 preterm infants, with a variable birthweight of 2 and 2.5 kg,. from which 5 are in the group of patients without a history of tuberculosis, 4 children had history of tuberculosis and 1 of them had a type of 'contact'. In order to exclude factors other than the purpose of the study, infants with tuberculosis, syphilis, congenital malformations, and constitutional alterations were not considered in the study.

Weight and height, as well as morbid incidence, were recorded in quarters. The infections were not considered separately, according to diagnoses or system affected, but, according to the purpose of obtaining only a panoramic view of this aspect of evolution, a general estimation of it was made. Any type of in-

fection, regardless of its nature, was counted, in which case it was also done, although separately for each of them, in case of simultaneous incidence of two or more conditions.

Regarding tuberculosis, their existence was excluded due to prolonged clinical observation and persistent negativity of the tuberculin series and radioscopic examination of the thorax. As a purely informative data, we must mention that 5 infants who had originally been selected for the study to fulfill the conditions stipulated in the plan, previously disclosed, were eliminated, due to developing the primoinfection during their stay at the institution. There was a history of contact with her tuberculous mother in all of them, by one month or so.

As for the medical and nursing care included in the study, it was not different from the one dispensed always in the establishment. We could disclosed more details at another time. The same should be noted regarding the process of elimination, strictly adhered to the pediatric canons that we are used to practice.

Results

These appear in the tables. If we focus our attention on table 1, we will find the weight values of the different groups in their different ages. We are fundamentally interested in whether the differences between the weights of the three groups are statistically significant, in other words, whether or not they can be explained by simple random variations.

As for the results of this statistical study for height, the values shown in table 2 were obtained. This measure is the same for all three series.

Both in the study of this variable and in that of weight, it is not possible to advance in the statistical calculation in infants older than 1 year due to the reduced number of observations.

With respect to the morbid incidence of the different groups (table 3), we used the unit of measure called the person-week to calculate the rates. In the first trimester, we can see 55 cases in the group of infants without a history of maternal tuberculosis, 44 in the separated group and 13 in the group of contacts who were exposed to the risk of becoming ill during a trimester. These figures are equivalent to a total of 660, 528 and 156 people exposed to the risk of illness for 1 week.

When calculating morbidity rates for the aforementioned age period, they result in 21.9%, 22.1% and 12.2%, respectively. The comparison between the percentages of the first two groups (sigma of difference) reveals that the difference between them is not statistically significant. As for the morbidity rate of the group of infants in contact, the reduced number of observations that integrate it does not allow progress in the statistical calculation. The above-mentioned operation, applied at the rates of the groups that follow, excluding those older than 1 year, for the same reason given for the infants in contact in their first trimester, does not show differences of statistical significance.

Table 1. Study of weight o infants with or without history of tuberculous mother. Servicio Asilo Hospital L. Calvo Mackenna. 1948

		Admission	3RD month	6°	9°	12°	15°	18°	24°
Group I (without history of TB)	n° cases	76	76	76	61	41	9	12	3
	Mean weight (Kg)	3.35	4.20	5.82	7.00	8.00	9.52	9.53	8.88
	SD	± 0.76	± 0.590	± 0.70	± 0.90	± 1.0			
Group II (separated from the TB mother)	n° cases	57	57	57	53	40	7	11	2
	Mean weight (Kg)	3.33	4.04	5.41	6.92	8.33	8.63	10.34	10.56
	SD	± 0.730	± 0.740	± 0.68	± 0.86	± 0.95			
Group III (in contact with TB mother)	n° cases	26	26	26	24	20	5	3	
	Mean weight (Kg)	3.70	4.30	5.71	7.11	8.12	9.66	9.56	
	SD	± 0.880	± 0.00	± 0.78	± 0.68	± 0.50			
OMS 2006 Males* Mean (± 1SD)			6.40 (5.70- 7.20)	7.9 (7.1-8.8)	8.9 (8.0-9.9)	9.6 (8.6-10.8)	10.3 (9.2-11.5)	10.9 (9.8-12.2)	12.2 (10.8-13.6)
OMS 2006 Females* Mean (± 1SD)			5.8 (5.2- 6.6)	7.3 (6.5-8.2)	8.2 (7.3- 9.3)	8.9 (7.9-10.1)	9.6 (8.5-10.9)	10.2 (9.1-11.6)	11.5 (10.2-13.0)

SD = standard deviation. *Reference Chart o World Health Organization, WHO 2006[9] (included in the review in the review of the manuscript).

Table 2. Study of height of infants with or without history of tuberculous mother. Servicio Asilo Hospital L. Calvo Mackenna. 1948

		Admission	3RD month	6º	9º	12º	15º	18º	24º
Group I (without history of TB)	nº cases	76	76	76	61	41	9	12	3
	Mean weight (Kg)	51.5	54	62	66	70	73	75	77
	SD	± 0.68	± 1.4	± 0.49	± 1.16	± 0.98			
Group II (separated from the TB mother)	nº cases	57	57	57	53	40	7	11	2
	Mean weight (Kg)	51	57	61	67	70	72	78	82
	SD	± 0.54	± 1.01	± 1.06	± 1.01	± 0.96			
Group III (in contact with TB mother)	nº cases	26	26	26	24	20	5	3	
	Mean weight (Kg)	53	56	61	66	70	75	77	
	SD	± 0.82	± 0.79	± 0.96	± 0.99	± 0.75			
OMS 2006 Males* Mean (± 1SD)			61.4 (59.4-63.5)	67.6 (65.5-69.8)	72.0 (69.7-74.2)	75.7 (73.4-78.1)	79.1 (76.6-81.7)	82.3 (79.6 -85.0)	87.8 (84.8-90.9)
OMS 2006 Females* Mean (± 1SD)			59.8 (57.7- 61.9)	65.7 (63.5- 68.0)	70.1 (67.7- 62.7))	74 (71.4- 76.6)	77.5 (74.8-80.2)	80.7 (77.8- 83.6)	86.4 (83.2-89.6)

SD = standard deviation. *Reference Chart o World Health Organization, WHO 2006[9] (included in the review in the review of the manuscript).

Table 3. Study of morbid incidence in infants with or without history of tuberculous mother. Servicio Asilo Hospital L. Calvo Mackenna. 1948

		1th trimester	2ª	3º	4º	5º	6º	7º y 8º
Group I (without history of TB)	nº cases	55	76	61	41	9	12	3
	Persons/week	660	912	732	492	106	144	27
	nº infections	145	263	232	128	28	63	16
Group II (separated from the TB mother)	nº cases	44	57	53	40	7	11	2
	Persons/week	528	684	636	480	84	132	24
	nº infections	117	219	203	131	29	58	9
Group III (in contact with TB mother)	nº cases	13	26	24	20	5	3	
	Persons/week	156	312	288	240	60	36	
	nº infections	19	67	76	73	16	12	

Commentary

The results previously described are consistent with those obtained by Bernard and Lelong. There are practically no differences in the development and general characteristics of evolution among infants born from tuberculous mothers and those who do not suffer from this condition. This finding, as well as the absence of positive tuberculin reactions in children of tuberculous mother, can be considered as new facts against Couvelaire's interpretation of the picture of progressive malnutrition. Considering this evidence, which are proven in other studies, his explanation can not be other than the hospitalism, which would be considered by Redeker and others.

Another observation taken from our material is the excellent result obtained by the separation method, since none of the infants integrating the group in which it was put into practice, developed tuberculosis. With this regard, it is possible to think, as Wallgren has especially emphasized, all the benefits that would be possible to obtain by simply keeping the child away from the infecting focus.

Commentary on Correa and Zenteno's article.

Since ancient times, TB has been a threat to global public health systems. In Chile, it was a problem

of extreme gravity during the 20th century, until control of the disease was achieved, reaching current mortality rates of 1.6/100,000 inhabitants[10], being the third country with the lowest incidence of TB in Latin America[11]. This path of TB elimination began with the implementation of universal public health measures through the National Health Service in 1952, adding the subsequent formulation of the National Program for Tuberculosis Control in the early 1970s, coupled with the improvement of life conditions of the entire population. Currently, it is focused on those vulnerable groups, such as immigrants, HIV carriers and those who are in prison[12].

This disease was described 1500 years ago by Hippocrates as "*tisis*" or "*consumpción*", due to the important nutritional commitment that experimented the patient. In a 1988 publication, Lewinson et al. described that a 28% of the children hospitalized for TB were malnourished, a rate that exceeded 16.5% of the reference population[13]. Probably, it was believed that a child birth from an infected mother conditioned a greater risk of anergy and progressive malnutrition, a hypothesis refuted in the Correa and Zenteno cohort, which with basic statistics showed that there are no differences in the incidence of infectious disease or growth between the group of children of the tuberculous mother and the control group. However, when compared to the current reference population, based on a large sample of children who have the conditions to reach their growth potential, it appears that the entire sample of institutionalized children in the 1940s had a severe staturo-ponderal compromise[9].

The authors also highlight the "*excellent results of the separation method, since none of the infants in the group in which it was implemented developed tuberculosis*." From the group of infants who remained with their mothers at birth for a period of at least 1 month, because they were born at home or because of a lack of quotas at the Hospital, five were excluded from the study, due to their development of the primoinfection during their stay in the establishment. It was recommended to stop the brestfeeding and to separate the child from his/her mother, because the mother is the main source of contagion[13]. The childcare booklet published in 1930 state: "*The child has **the right** to be breastfeed by the mother, and it does not bring any harm to the woman who rears. Only tuberculosis, serious diseases of heart and kidneys and some contagious diseases force to remove the breast. Back pain or other mild discomforts such as general weakness are not grounds for discontinuing breastfeeding*"[4].

The indication of separating the child from the bed of his/her mother would have been maintained in some countries until the end of the 20th century[14]. Nevertheless, thanks to the demonstration of the possibility of treatment of pregnant women without risk to the embryos in formation and the effectiveness of prophylaxis in newborns, this practice became obsolete. In our country, the Technical Regulations for the control and elimination of tuberculosis, published by the Ministry of Health Chile 2014[15] recommends the use of masks and chemoprophylaxis to newborns of mothers with pulmonary tuberculosis and treatment in case of newborns who are clinically ill or suspected of having congenital tuberculosis.

To take care of the dyad, as well as the promotion of attachment and breastfeeding are fundamental for the child care and well-being. The first time that the incorporation of the mother in an hospitalized child's care was mentioned in our country was back in 1937[16], and it showed all the evidence, almost intuitively collected, about the harmful effect of "*hospitalism*" on the nutritional and emotional development of the children[17,18]. This visionary recommendation took 50 years until it was possible to apply, integrating the family in the care of the children[19]. With public health measures such as this, Chile has improved its quality of life, and it has conquered in less than a century, not only epidemics such as tuberculosis and infant mortality, but also the right of the child to be close to his/her mother.

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