Chilean School-Age Children Twin Registry: Planning, Sampling and Implications

Daniza M. Ivanovic,[1,2,6] Elena R. Llop,[3] Jorge A. Alvear,[1] Hernán T. Pérez,[1] Nora S. Díaz,[1] Bárbara D. Leyton,[1] Atilio F. Almagià,[4] Cristián G. Larraín,[5] Joel E. Alvarez,[2,6] Yilda F. Herrera,[1] and Elizabeth L. Hazbun[1]

[1] *Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile*
[2] *School of Public Health, Loma Linda University, California, United States of America*
[3] *Institute for Biomedical Sciences, Human Genetic Program, University of Chile, Santiago, Chile*
[4] *Catholic University of Valparaíso, Valparaíso, Chile*
[5] *Department of Magnetic Resonance Imaging Service, German Clinic of Santiago, Santiago, Chile*
[6] *Adventist University of Chile, Chillán, Chile*

We describe subject recruitment from the University of Chile School-Age Children Twin Registry (REMEUCHI). The research aim of REMEUCHI is to quantify the impact of genetic and environmental factors on scholastic achievement in a multicausal approach. The Ministry of Education of Chile, in collaboration with the Registry Office, provided the list of possible twin pairs graduated from high school in 2004 in Chile's metropolitan region. From a population of 70,065 school-age children who had graduated from high school, 434 possible twin pairs were analyzed. Of these, 327 were twins reared together (75.3% of the 434 possible twins pairs) and born between 1986 and 1987 in Chile (mean age 18 years), and approximately 8% were not twins despite matches on full name and birth data. The rest of the possible twin pairs were probably twins reared apart, since one member of the pair had moved to study in another region of Chile. Zygosity was determined through questionnaires, maternal reports of twin similarities, and by the hospital records of the twins at the time of birth. Three hundred and twenty-seven pairs were identified, where monozygotic (MZ) and dizygotic (DZ) twins represented 46.8% and 53.2% of pairs, respectively, with a DZ/MZ ratio of 1.14. Considering same-sex MZ pairs, the percentage of female pairs was greater (55.6%) than male pairs (44.4%). When DZ pairs were analyzed, 47.7% were of opposite sex, 20.1% were male pairs and 32.2% female pairs. In Chile, these findings represent a baseline study to contribute to the establishment of a national twin registry in the future.

Previous findings demonstrate that the learning process is conditioned by genetic and environmental factors (Ivanovic et al., 2002, 2004, 2006). In Chile, research related to the impact of genetic and environmental factors on the learning process in a multicausal context is nonexistent. Twin studies offer an adequate research design to assess these aspects and, in this context, research on monozygotic (MZ) and dizygotic twins (DZ) is especially relevant as these are the only studies that allow better clarification as to the relative weight of genetic and environmental factors in these interrelationships. Multicausal studies carried out with the aim of determining the explanatory power of genetic and environmental factors in the interrelationships between educational, intellectual, nutritional, brain development, socioeconomic, sociocultural, family and demographic variables, face a serious obstacle since there is no twin registry of any age group in Chile, and this has prevented research in this area. Twin research has the greatest power for the genetic analysis of complex multifactorial traits and diseases in humans. Modern twin analyses extend beyond the classical twin study for estimating the heritability of a trait (Busjahn, 2002).

In many countries, twin registries are an important resource for genetic and epidemiologic studies of common and complex diseases (Boomsma et al., 2002). Twin registers are established worldwide to study the role of genes and environment in different aspects of health and behavior.

The Sri Lanka Twin Registry is the first in the developing world (Sumathipala et al., 2003). In Chile, as well as in Latin American and Caribbean countries, twin studies are mainly related to clinical aspects or case studies, and not twin registries (Beiguelman et al., 2000; Briceño & Briceño, 2005; Colletto, 2003; Daher et al., 1991; Daré et al., 1993; Nazer et al., 1999, 2006).

In 2004 we began a study focused on determining the impact of genetic and environmental factors in the interrelationships between scholastic achievement, intelligence, nutritional status and brain development in MZ and DZ Chilean school-age twins reared

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Address for correspondence: Prof. Daniza Ivanovic, University of Chile, Institute of Nutrition and Food Technology (INTA), Santiago, Chile. E-mail: daniza@inta.cl; inta8@abello.dic.uchile.cl

together and who had completed high school in the metropolitan region. As there were no existing twin registries in Chile, the first national twin registry was established in 2004.

The Database of Possible Twins

Population

The Ministry of Education of Chile, in collaboration with the National Registry Office, provided a list of school-age children who were possibly twin pairs, and who had graduated from high school in Chile's metropolitan region including the capital city. The children in the list were sorted by surname and birth date. This yielded a total of 1173 possible twin pairs in the country; approximately one third (434 possible twin pairs) were living in the metropolitan region. The list included the complete names of the possible twin pairs, their national identification number, date of birth, educational achievement, and the name of the high school from which they had graduated as well as its address, telephone number and the county in which it was located.

Location of the Twins

The list was used as the basis for the twin registry. We either visited each educational establishment or sent e-mails, in order to verify the information provided by the Ministry of Education and the National Registry Office. We updated the address, telephone, e-mail and district in which the home of each possible twin pair was located; when the telephone number did not correspond to the twin's family, the house was visited in order to further validate the information.

Recruitment

Personal contact was established with each family with the purpose of interviewing the twin pair and their mother at home in order to determine zygosity; they were informed in detail about the aim of the research. If the pair agreed to participate in this investigation, they signed the informed consent form as per the norms for Human Experimentation, Code of Ethics of the World Medical Association (Declaration of Helsinki; The World Medical Association 1964). Twins showed a strong interest in participation, and the positive response rate was very high (95%); despite this level of interest, full-time jobs or university studies were the most common reasons given for declining to participate in this study.

Zygosity Study

Zygosity was determined by questionnaire (Lykken et al., 1990), considering that in Chile most of the population has European ancestry, with variations in hair and eye color. In the same way, the birth records at the hospital where the twins were born were reviewed to determine whether the pair was MZ or DZ, and information on the mother was also recorded. Hospital birth records were not very accurate as they only registered birthweight, birth length, head circumference, Apgar score, the order of the twin's birth (first or second) and, in some cases, whether the pair had one or two placentas.

Current Sample

Of the 434 possible twin pairs, we identified 327 reared-together twin pairs (75.3%) who were born between 1986 and 1987 (mean age 18 years). Approximately 8% were not twins despite matching last names and birth data. The remaining possible twin pairs were probably twins reared apart, since one member of the pair lived and studied in a different region of Chile. This needs further investigation since some families who reported twins who were reared apart did not give the reasons. In addition, three triplets were located, one all-male triplet and two triplets formed by two males and one female.

The zygosity questionnaire data was in good agreement with information given by the mother and in some pairs, by the birth records of the hospitals. Only two cases had discrepancies between the questionnaire and the information obtained from the mother. In these cases, data from the birth records of the hospital was relied upon.

In Table 1, gender and zygosity is given for twins who were reared together and who graduated from high schools in the metropolitan region in 2004. Of the pairs, 46.8% were MZ and 53.2% were DZ, with a DZ/MZ ratio of 1.14. Considering same-sex MZ pairs, the proportion of female pairs was greater (55.6%) than male pairs (44.4%). When DZ pairs were further analyzed, 47.7% of the total DZ twin pairs were of opposite sex, 20.1% were male pairs and 32.2% were female pairs.

Discussion

Setting up a twin registry in Chile has presented a difficult task. This is due mainly to migration, country to city migration, rural development, and relocation, which result in changes in contact details (address and telephone) which interfere with the tracing of twins from school record addresses.

During 2004, 70,065 school-age children graduated from high school in the Metropolitan Region (38% of the Chilean school population) of whom

Table 1

Twins Registered in the Chilean School-Age Children Twin Registry by Sex and Zygosity

	MZ		DZ		Total	
	n	%	*n*	%	*n*	%
Male-Male	68	44.4	35	20.1	103	31.4
Female-Female	85	55.6	56	32.2	141	43.2
Opposite sex	—	—	83	47.7	83	25.4
Total	153	100.0	174	100.0	327	100.0

Note: MZ = monozygotic twins; DZ = dizygotic twins.

approximately 1% were twins, since 327 reared-together twin pairs (654 school-age individual twins) were found. This is in agreement with the twinning rate of European countries and the United States, approximately 1.1 to 1.2% of deliveries (Becker, 1971; Boomsma et al., 2002; Hall, 2003; Lenz & Lenz, 1971).

The findings of this study showed that the DZ/MZ ratio was 1.14; there are no other studies in Chile to compare this rate with. Twinning rates in developed as well as developing countries have been shown to be on the increase. Although the frequency of MZ twinning has remained constant, DZ/MZ ratios vary in the different countries (Imaizumi, 2003). The maternal age at birth has partially contributed to the increase in the proportion of multiple births. This evolution in twinning rate has been impacted by the mothers' age, as compared to younger mothers, older women tend to have twins more frequently. Moreover, the increasing frequency of multiple births is also impacted by fertility treatments, which are widely used in developed countries (Beemsterboer et al., 2006; Duccini dal Colletto et al., 2001; Goswami & Goswami, 1993; Hur & Kwon, 2005; Imaizumi, 2003; Pison & D'Addato, 2006; Tong et al., 1997). Other authors report that with advancing maternal age, fertility declines but simultaneously twinning rates increase (Beemsterboer et al., 2006).

Zygosity is influenced by many factors. MZ twins occur spontaneously in approximately 1 in 250 births and are felt to increase twofold with ovulation induction techniques. MZ twinning also increases in proportion to the number of blastocysts transferred during in vitro fertilization (Hankins & Saade, 2005). In contrast, DZ twinning appears to be influenced by race, genetic factors, maternal age, fertility enhancing drugs, folic acid supplementation, and maternal nutritional status (Hankins & Saade, 2005). In addition, changes in twinning and triplet rates by zygosity have been observed in many countries (Imaizumi, 2003). Several investigators have found that the rate of MZ twinning has remained fairly constant around the world, with variability being attributable to the rate of DZ twinning, so that the ratio of MZ to DZ twinning varies strikingly (Hall, 2003; Kiely & Kiely, 2001; Murphy & Hey, 1997; Nylander, 1975).

Several authors have highlighted that approximately one third of twins are MZ (Becker, 1971; Hall, 2003; Lenz & Lenz, 1971), however in this sample, MZ twins represented 46.8% of the total sample. The proportion of opposite-sex DZ twins is approximately the same as same-sex DZ twins, in agreement with Weinberg's method (Weinberg, 1902); however, the percentage of MZ twins was double the percentage of DZ twins of the same sex. Regarding the proportion of same-sex to opposite-sex twins, male pairs to female pairs to opposite-sex pairs were 1:1:2. Female twins are more likely to be the product of MZ twinning than male twins in this study, as found in other studies (Basso et al., 2004; James, 1971, 1980). This was also observed in DZ twins.

These findings form a baseline study that contributes to the setting up of a national twin registry. A representative, stratified and proportional sample of 140 twin pairs was randomly chosen from the 327 pairs in 2006. Currently, nutritional, intellectual, personality, socioeconomic, sociocultural, family, mass media exposure, demographic and educational parameters are being assessed in this sample and it is planned to repeat the same procedure every 5 years. In addition, we are working with the Ministry of Education to increase the University of Chile School-Age Children Twin Registry (REMEUCHI) to include school-aged children from infant school to high school.

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