Twin Research and Human Genetics (2021), **24**, 133–139
doi:10.1017/thg.2021.12

CAMBRIDGE UNIVERSITY PRESS

Article

Maternal and Perinatal Factors Associated With Twin Pregnancies in Ecuador

Ximena Orozco-Quinga[1] and Fabricio González-Andrade[1,2]

[1]Universidad San Francisco de Quito USFQ, Colegio Ciencias de la Salud, Quito, Ecuador and [2]Universidad Central del Ecuador, Facultad de Ciencias Médicas, Unidad de Medicina Traslacional, Quito, Ecuador

Abstract

There are few studies on twins in Ecuador and Latin America. It requires a better understanding of perinatal conditions, especially from an ethnic perspective. This work aims to assess perinatal factors related to twin pregnancy in Ecuadorian Mestizo individuals. We performed an epidemiological, observational and cross-sectional study at the Hospital San Francisco and Hospital Nueva Aurora in Quito, Ecuador, from November 2019 to January 2020. It included 203 newborns from twin pregnancies, including mothers with and without pathological history. The average gestational age was 31 weeks, and the APGAR score at first minute was 6.86, with significant differences. Regarding the metabolic balance, the mean pH was 6.14; and bicarbonate was 11.57, with significant differences. Twins had intrauterine growth restriction in 6.9% of cases, with significant differences ($p = .003$); 81.4% required supplemental oxygen, with significant differences ($p = .002$); 93% required non-invasive mechanical ventilation (NIMV), with significant differences ($p = .003$); 93% required inotropic and sedation, with substantial differences; 69% required antibiotics (≥21 days), with significant differences ($p = .014$); and 17.2% needed between 8 to 14 days of hospitalization, and 51% more than 28 days, with significant differences. The studied mothers' demographic profile was mostly Mestizos, with an average age of 32 years, and 93% had a poverty status. Most of the twins were diamniotic monochorial and were discordant twins. It found jaundice, premature anemia and sepsis in 100% of twins and hyaline membrane disease in 89.66% of twins. Twins of women with relevant prenatal care had more premature births (30.4 ± 2.6 weeks), more acid–base imbalance, APGAR at ≥7 min in 90% of cases, and patent ductus arteriosus in all. There was also a greater need for double intensive phototherapy than twins of healthy women.

Keywords: Twin pregnancy; perinatal care; patent ductus arteriosus; family medical history; ethnicity; Mestizos; Ecuador; Latin America

(Received 21 January 2021; accepted 16 February 2021; First Published online 23 March 2021)

Multiple pregnancies represent 2–4% of the total number of births worldwide; they have increased notably in the last 30 years due to a more advanced maternal age and greater use of assisted reproductive technology (ART; Santana et al., 2018). Twin pregnancies account for 3% of live births and 96% of multiple births. Dizygotic (DZ) twins are more common than monozygotic (MZ) twins, with a ratio of 70:30, but this relationship changes according to every population (Wei et al., 2016). There is a vanishing twin phenomenon where a significant percentage of twin pregnancies, especially from ART, later become singleton pregnancies (Berceneau et al., 2018).

The multiple birth rate has increased by more than 20% in the USA, 15% in South Korea and 29% in Denmark (Chen et al., 2019). To our knowledge, there are few studies on twins and twin pregnancies in Ecuador and Latin America (Ganchimeg et al., 2014; Leimberg et al., 2009; Naranjo-Espín & Calle-Miñaca, 2019). There are no twin registries in Ecuador. A better understanding of perinatal conditions is needed. Additionally, Ecuador has a unique characteristic because it is a multi-ethnic country with larger cities located at high altitudes 2500 meters above sea level (González-Andrade, 2020). These issues, of course, may influence perinatal conditions affecting newborns.

Adaptation to a twin pregnancy leads to various complications (Committee on Practice Bulletins-Obstetrics, & Society for Maternal-Fetal Medicine, 2016). For example, maternal death rates associated with a twin pregnancy are 2.5 times greater than a singleton pregnancy (Leimberg et al., 2009), and advanced age is associated with an increased risk of preterm delivery, fetal death, chromosomal abnormalities and maternal complications (Esteves-Pereira et al., 2021). In the same way, there is a higher risk of miscarriage, hemorrhagic complications, anemia and polyhydramnios in twin pregnancies (Rissanen et al., 2019a). Preeclampsia is three times more common in multiple pregnancies than in singleton pregnancies and is likely to be more severe (Smith et al., 2014). The perinatal mortality rate is two to three times higher in twins due to premature delivery, fetal growth restriction, low birth weight and intrapartum anoxia (Hviid et al., 2018). Neonatal jaundice and sepsis are also common complications. If the twins are also discordant, there is a higher frequency of sepsis (McLennan et al., 2017), and this factor increases the need for mechanical ventilation for extended periods (Martinka et al., 2019; Ndiaye et al., 2018).

From an epidemiological perspective, increased maternal age causes one-third of spontaneous DZ twins. Afro-descendants have

Author for correspondence: Fabricio González-Andrade, Email: fabriciogonzaleza@gmail.com

Cite this article: Orozco-Quinga X and González-Andrade F. (2021) Maternal and Perinatal Factors Associated With Twin Pregnancies in Ecuador. *Twin Research and Human Genetics* **24**: 133–139, https://doi.org/10.1017/thg.2021.12

the highest DZ twinning rates and Asian descendants the lowest (Monden & Smits, 2017). Increased parity is associated with increased twinning. Having a maternal family history of DZ twins increases the likelihood of twins (Rissanen et al., 2019b). Furthermore, morbidity and mortality are higher in twins than in singleton pregnancies (Monahagan et al., 2019). Twin pregnancies have a higher risk of preterm birth, lower birth weight and growth restriction (Sabatelli et al., 2019; Townsend & Khalil, 2018). They are also more likely to have congenital defects, especially in MZ twins. Finally, twinning increases the rate of fetal and neonatal death (Ghi et al., 2019).

This article assesses the perinatal factors related to twin pregnancy in Ecuadorian Mestizo individuals.

Methods

Research Design

We followed an epidemiological, cross-sectional and observational design with two cohorts of multiple pregnancies.

Settings

We performed this research at Hospital San Francisco and Hospital Luz Elena Arismendí, both in Quito, Ecuador, from November 2019 to January 2020.

Participants

Participants were two cohorts of twin newborns, split by the presence or absence of prenatal pathologies. The study population was preterm infants born between 25 weeks and 37 weeks of gestation, admitted to two public hospitals' neonatology units. We made the ethnic identification considering self-identification, the origin of the surnames, the language spoken, the place of birth, and the ancestors' surnames and origin. There were 203 neonates in the study.

Variables

We analyzed prenatal factors such as age, socioeconomic status, education level and the number of prenatal controls. We also considered lung maturation, infections, premature rupture of the membranes, chorioamnionitis, anemia, gestational diabetes, infections, hypertensive disorders of pregnancy, bleeding, fetal fetus transfusion syndrome and fetal wellness compromise. Perinatal factors analyzed were gestational age, birth weight, sex, ethnicity, perinatal asphyxia, intrauterine growth restriction (IUGR), respiratory distress syndrome, jaundice, sepsis, anemia, the persistence of ductus arteriosus and neonatal shock.

Data Sources

Researchers compiled information from the medical records, which included prenatal and perinatal data, information on the birth and progress of the hospitalization of neonates of twin pregnancy. To avoid bias, we recorded information in a datasheet, including maternal history and perinatal morbidities of twin pregnancy.

Statistical Methods

We analyzed data using SPSS© software version 22.0. We used descriptive and inferential statistics to compare maternal characteristics according to maternal history, natal characteristics according to the presence or absence of prenatal history, postnatal characteristics concerning the presence or absence of prenatal history, and the multivariate relationship between groups with or without a prenatal maternal history based on categorical principal components multivariate analysis (CATPCA). We accepted statistical significance with a p value of less than .05, chi-squared.

Exposure and Event to be Determined

The authors considered the variable of exposure to the presence or absence of fetal morbidities in twin pregnancies.

Ethical Approval

The Human Research Ethics Committee (CEISH) of the San Francisco University of Quito approved this research on November 15, 2019, study code: CA-P2019-159TPG-CEISH-USFQ.

Results

Table 1 shows descriptive statistics for maternal history. It describes that 34% had a significant prenatal history and 65.5% had no relevant history. The mothers' average age was 32 years; the average age was 33 years for mothers with a pathological prenatal history versus 31.4 years for mothers with no history; 93% of the mothers presented with some level of poverty; 93% of the mothers had at least five prenatal controls, recommended by the World Health Organization (WHO); 37.9% of the mothers showed vaginosis, without having statistically significant differences; 60% presented with hemorrhage and 40% with preeclampsia. According to maternal medical history, 20.6% of the pregnancies were diamniotic bichorial and 40% of mothers had a pathological prenatal history versus 10.5% for mothers without a prenatal history; 27.5% had diamniotic monochorionic pregnancies. In addition, 20.6% had multiple monoamniotic monochorial pregnancies; 37.9% were discordant twins; 20% were mothers with a prenatal history versus 47.3% without a prenatal history; and 34.4% presented with a commitment to the clinical wellbeing of the fetus. The birth weight discordance in twins found a weight difference between two twin brothers of at least 15%. Overall, we found 37% of twins with birth weight discordance.

Table 2 shows the distribution of natal characteristics according to the presence or absence of pathological prenatal history. The average gestational age was 31 weeks; mothers with a prenatal history had newborns of 30.3 weeks versus 31.1 weeks for mothers without a prenatal history. The mean birth weight was 1,208.6 g, 51.7% were female and 48.2% male, without statistical differences. Most individuals were Mestizos (86%), and we observed significant differences in ethnicity when comparing the presence or absence of prenatal history. We made the ethnic identification considering self-identification, the origin of the surnames and the language spoken, place of birth, and ancestors' surnames and origin.

When comparing prenatal medical history, 27.5% presented with asphyxia without substantial differences. The APGAR scale at 1 min, 5 min and 10 min was 6.86, 8.52 and 8.55, respectively. The mean APGAR at 1 min was 7.7 in mothers with a pathological prenatal history versus 6.4 in the other group. At 5 min, it was 8.8 in mothers with a prenatal history versus 8.3 in mothers without a prenatal history. The APGAR at 10 min was 8.9 in mothers with a prenatal history versus 8.3 in the other group. When considering an APGAR cutoff point of ≥7, we observed significant differences at 1 min; that value was for 90% of mothers without a history versus 67.4% for mothers with a history. Regarding metabolic balance, the

https://doi.org/10.1017/thg.2021.12 Published online by Cambridge University Press

Table 1. Descriptive statistics of maternal characteristics according to prenatal maternal history

Maternal characteristics	Total	Prenatal maternal history		*p*-Value
		Present	Absent	
Average age (*SD*)[1/] — years	32.09 (6.08)	33.23 (5.66)	31.49 (6.22)	.046*
Socioeconomic status, *n* (%)[2/]				
Middle class	14 (6.90)	14 (20.00)	0 (.00)	.000**
Poverty	189 (93.10)	56 (80.00)	133 (100.0)	
Recommended prenatal controls, *n* (%)[2/]				
Incomplete	14 (6.90)	0 (.00)	14 (10.53)	.001**
Complete	189 (93.1)	70 (100.0)	119 (89.47)	
Vaginosis, *n* (%)[2/]	77 (37.93)	21 (30.00)	56 (42.11)	.091
Maternal complications, *n* (%)				
Preeclampsia (hypertensive disorders of pregnancy)		28 (40.00)		
Hemorrhage		42 (60.00)		
Multiple pregnancy: classification, *n* (%)[2/]				
Biamniotic bicorial	42 (20.69)	28 (40.00)	14 (10.53)	.000**
Biamniotic monocorial	56 (27.59)	14 (20.00)	42 (31.58)	.079
Monocorial monoamniotic	42 (20.69)	0 (.00)	42 (31.58)	.000**
Discordance of birth weight in twins	77 (37.93)	14 (20.00)	63 (47.37)	.000**
Commitment to clinical fetal wellness, *n* (%)[2/]	70 (34.48)	28 (40.00)	42 (31.58)	.230

Note: *significant differences in means, [1/]based on *t* test; **significant differences in proportions, [2/]based on the test of homogeneity of the chi-square statistic; significance $p < .05$. The discordance of weight at birth in twins implies the existence of a weight difference between the two twin brothers of at least 15%. Recommended prenatal controls by World Health Organization means at least five controls during pregnancy.

mean pH was 6.14; there were no significant differences observed when comparing the presence or absence of prenatal history. Regarding PaCO2, the mean was 58.4, with substantial differences between the presence or absence of prenatal history ($p = .001$); the mean of PaCO2 was 40 for mothers with a history versus 61.5 for mothers with no history. If we take PaCO2 ≥ 58.4 as the cutoff point, there are significant differences; this value was found in 50% of mothers without a history, and no mothers with a history reached this value ($p = .015$). PaO2 had a mean of 43.5 without significant differences when comparing prenatal history's presence or absence. The mean of bicarbonate was 11.57, with significant differences when comparing the presence or absence of a prenatal history; if we take a bicarbonate cutoff point ≥ 11.5, there are also significant differences. The excess of base presented a mean of −15.7, with significant differences ($p = .000$); in mothers with prenatal history it was −12 versus −16.33 for mothers without a prenatal history. The mean of SatO2 (oxygen saturation) was 60.7, with significant differences ($p = .039$) in mothers with prenatal history; the mean of SatO2 was 56% versus 61.5% for mothers without a history.

Table 3 shows the distribution of postnatal characteristics of the presence or absence of pathological prenatal history: 6.9% had IUGR and we found differences when comparing the prenatal history — there were no cases of IUGR in mothers with a pathological prenatal history versus 10.5% without a pathological prenatal history; 3.4% of neonates had persistent ductus arteriosus, and 10% were neonates from mothers with a pathological prenatal history versus no cases for mothers with no history; 81.4% required supplemental oxygen; 70% were from mothers with a pathological prenatal history versus 88.2% from mothers with no history; 93% required noninvasive mechanical ventilation (NIMV), and 100% of these neonates were from mothers with a pathological prenatal history versus 89.4% from mothers with no history; 89% required simple phototherapy and 10.34% required double intensive phototherapy.

During their hospital stay, 93% of neonates required inotropic drugs or sedation and showed significant differences compared with pathological prenatal history, 100% for mothers with a history versus 89.4% for mothers with no history; 69% of the neonates required antibiotics for more than 21 days. Regarding antibiotics prescribed for less than 21 days, 20% were for mothers with a pathological prenatal history versus 36.8% from mothers with no history.

Figure 1 shows the multivariate relationship between groups with or without prenatal maternal history. We used a multivariate analysis of principal categorical components to determine the relationships between the variables. In this way, we characterized the groups by the presence or absence of pathological prenatal history, with phototherapy, APGAR at first minute, IUGR, supplemental oxygen and days with antibiotics. Dimension 2 discriminates between the groups of presence or absence of prenatal history. We observed the following: quadrant I and II characterize mothers without prenatal history related to simple phototherapy, IUGR, APGAR at first minute <7, supplemental oxygen and <21 days of antibiotic treatment. Quadrants III and IV characterize mothers with pathological prenatal history related to double intensive phototherapy, absence of IUGR, APGAR at 1 min ≥7, without supplemental oxygen, and who required ≥21 days with antibiotics.

Discussion

The twin pregnancy rate has increased in recent years due to greater access to fertilization techniques and the tendency to delay

https://doi.org/10.1017/thg.2021.12 Published online by Cambridge University Press

Table 2. Distribution of natal characteristics according to the presence or absence of prenatal history

Characteristics at birth	Total	Prenatal history		*p*-Value
		Present	Absent	
Gestational age, mean (*SD*)[1/] weeks	30.90 (2.37)	30.36 (2.56)	31.19 (2.21)	.017*
Birth weight, mean (*SD*)[1/] grams	1208.63 (364.12)	1215.24 (384.1)	1205.15 (354.6)	.852
Sex, *n* (%)[2/]				
Male	98 (48.28)	35 (50.00)	63 (47.37)	.721
Female	105 (51.72)	35 (50.00)	70 (52.63)	
Ethnicity, *n* (%)[2/]				
Mestizo	175 (86.21)	56 (80.00)	119 (89.47)	.000**
Afro-Ecuadorians	14 (6.90)	0 (.00)	14 (10.53)	
Native Amerindians	14 (6.90)	14 (20.00)	0 (.00)	
Perinatal asphyxia, *n* (%)[2/]	56 (27.59)	14 (20.00)	42 (31.58)	.079
APGAR 1 min, mean (*SD*)[1/]	6.86 (2.05)	7.7 (.64)	6.42 (2.38)	.000*
APGAR 5 min, mean (*SD*)[1/]	8.52 (.73)	8.8 (.4)	8.37 (.81)	.000*
APGAR 10 min, mean (*SD*)[1/]	8.55 (.73)	8.9 (.3)	8.37 (.81)	.000*
APGAR 1 min ≥7, *n* (%)[2/]	154 (75.86)	63 (90.00)	91 (67.42)	.001**
APGAR 5 min ≥7, *n* (%)[2/]	196 (96.55)	70 (100.00)	126 (94.74)	.098
APGAR 10 min ≥7, *n* (%)[2/]	196 (96.55)	70 (100.00)	126 (94.74)	.098
pH, mean (*SD*)[1/]	6.14 (.35)	7 (-)	6 (-)	–
PCo2, mean (*SD*)[1/]	58.43 (16.85)	40 (.00)	61.50 (16.28)	.001*
PCo2 ≥ 58.43, *n* (%)[2/]	21 (42.86)	0 (.00)	21 (50.00)	.015**
PaO2, mean (*SD*)[1]/	43.57 (13.07)	43 (.00)	43.67 (14.14)	.762
HCO3, mean (*SD*)[1/]	11.57 (2.58)	7.00 (.00)	12.33 (1.91)	.000*
HCO3 ≥ 11.57, *n* (%)[2/]	28 (57.14)	0 (.00)	28 (66.67)	.001**
Base excess/deficit, mean (*SD*)[1/]	−15.71 (4.57)	−12 (.00)	−16.33 (4.55)	.000*
3 ≥ −15.71, *n* (%)[2/]	21 (42.86)	7 (100.00)	14 (33.33)	.001**
SatO2, mean (*SD*)[1/]	60.71 (15.54)	56 (.00)	61.50 (16.68)	.039*
SatO2 ≥ 60.71, *n* (%)[2/]	14 (28.57)	0 (.00)	14 (33.33)	.170

Note: *significant differences in means, [1/]based on *t* test; **significant differences in proportions, [2/]based on the analysis of homogeneity of the chi-square statistic; significance $p < .05$.

motherhood. We carried out this investigation to determine the effect of maternal clinical history and its relationship with perinatal complications in twin pregnancies. The average age in both cohorts was less than 35 years. Maternal age showed statistically significant differences. Women with pathologies during pregnancy, such as hypertensive disorders of pregnancy, including chronic hypertension, preeclampsia-eclampsia and preeclampsia added to chronic hypertension, gestational hypertension and bleeding during pregnancy had a higher mean age between both groups. This variable is a factor associated with an increased risk of premature delivery, fetal death, fetal aneuploidy and increases in multiple pregnancies.

Regarding admixture genetic studies in non-twins, González-Andrade et al. (2007) analyzed autosomal microsatellites and found that Mestizos have 73% Amerindian DNA, 19% European Caucasian and 8% African, while Afro-descendants are 56% African, 28% Amerindian and 16% European. In relation to the genetic markers of the Y-chromosome, which shows the Conquest side, the Mestizos have 70% European Caucasian DNA, 28% native Amerindian and 2% African; while Afro-Ecuadorians have 44% African, 31% European DNA and 15% Amerindian. A study by Santangelo et al. (2017) using genetic markers of ancestry (AIMs) found that current Mestizos have 66% native DNA Amerindian, 30% European Caucasian and 4% African. Afro-Ecuadorians showed 59% African DNA, 28% Native American and 13% Caucasian. Finally, the Kichwas showed 91.5% Amerindian DNA, 7% European DNA and 1.5% African DNA.

Regarding the socioeconomic level, poverty was predominant in both groups because the research was conducted in two public hospitals in Quito that draw their patients from a lower socioeconomic stratum. All women with a medical history received complete prenatal care, with at least five prenatal controls. Concerning ethnicity, significant differences were found: pregnant women presented higher fetal pathologies, a factor related to less access to health services and actions to promote health and a healthy lifestyle.

On the other hand, many varieties of multiple pregnancies evidenced statistically significant differences according to pathologies during pregnancy; for example, diamniotic bichorial pregnancy was more frequent than in singleton pregnancies. In contrast, monochorionic pregnancy was more prevalent in women without a prenatal clinical history. Monochorionic pregnancies have an

https://doi.org/10.1017/thg.2021.12 Published online by Cambridge University Press

Table 3. Distribution of postnatal characteristics concerning the presence or absence of pathological prenatal history

Postnatal characteristics	Total	Prenatal history		*p*-Value
		Present	Absent	
Intrauterine growth restriction, *n* (%)[2/]	14 (6.90)	0 (.00)	14 (10.53)	.003*
Hyaline membrane disease, *n* (%)[2/]	182 (89.66)	63 (90.00)	119 (89.47)	.907
Jaundice, *n* (%)[2/]	203 (100.00)	70 (100.00)	133 (100.00)	1.000
Premature anemia, *n* (%)[2/]	203 (100.00)	70 (100.00)	133 (100.00)	1.000
Sepsis, *n* (%)[2/]	203 (100.00)	70 (100.00)	133 (100.00)	1.000
Patent ductus arteriosus, *n* (%)[2/]	7 (3.45)	7 (10.00)	0 (.00)	.000*
Supplemental oxygen, *n* (%)[2/]	154 (81.48)	49 (70.00)	105 (88.24)	.002*
Noninvasive mechanic ventilation — NIMV, *n* (%)[2/]	189 (93.10)	70 (100.00)	119 (89.47)	.003*
Invasive mechanic ventilation, *n* (%)[2/]	175 (86.21)	56 (80.00)	119 (89.47)	.086
Phototherapy, *n* (%)[2/]				
Simple	182 (89.66)	49 (70.00)	133 (100.00)	.000*
Double	21 (10.34)	21 (30.00)	0 (.00)	
Inotropic use, *n* (%)[2/]	189 (93.10)	70 (100.00)	119 (89.47)	.003*
Sedation, *n* (%)[2/]	189 (93.10)	70 (100.00)	119 (89.47)	.003*
Days of antibiotics, *n* (%)[2/]				
<21 days	63 (31.03)	14 (20.00)	49 (36.84)	.014*
≥21 days	140 (68.97)	56 (80.00)	84 (63.16)	
Hospital stay days, *n* (%)[2/]				
8–14 days	35 (17.24)	21 (30.00)	14 (10.53)	.001*
15–28 days	63 (31.03)	14 (20.00)	49 (36.84)	
>28 days	105 (51.72)	35 (50.00)	70 (52.63)	

Note: *significant differences in proportions, [2/]based on the chi-square statistic test for homogeneity; significance $p < .05$.

increased risk of stillbirth, genetic abnormalities, premature delivery and IUGR compared to dichorionic twins. This monochorionic condition presents a higher risk because there is an asymmetric distribution of the placental mass, defects in the placental vessels' anastomoses and even the possibility of nonviable congenital anomalies. Furthermore, twin-to-twin transfusion syndrome is quite common and affects 10–15% of monochorionic twins. This syndrome, without treatment, causes perinatal death in 70–90% of cases. In addition, there is an increased risk of IUGR and discordance in the growth of twins.

There were no differences in either of the two cohorts regarding the variables of bacterial vaginosis and fetal wellbeing. These findings mean that maternal medical history is not related to these events. Other variables studied were hypertensive disorders of pregnancy, infections and fetal distress secondary to a twin pregnancy due to high hormone levels, and hypovolemia and overdistension of the uterus, but there were also no differences in these variables. Women with multiple pregnancies have immunity deficits mediated by T-helper lymphocytes type 1 and 2, limitation in activation of macrophages, B lymphocytes and CD8 compared to single pregnancies, and increased risk of developing infectious complications.

Thus, hemorrhagic complications were more frequent in pregnant women with a prenatal history. A clear association with hypertensive diseases described a higher probability of retroplacental hematomas; however, we established no significant associations between these pathologies and maternal history in our study population. Likewise, the commitment to fetal welfare was more frequent in neonates of pregnant women with a clinical history, especially hypertensive disease and diabetes, factors that did not show statistically significant associations in our study and should be analyzed in a larger sample.

Gestational age was lower in newborns of women with comorbidities during pregnancy, and this causes prematurity. Thus, factors such as stretching of the cervix elevated placental corticotropin-releasing hormone levels, and we observed lung maturity factor in prematurity. Prematurity itself causes respiratory distress, patent ductus arteriosus, intraventricular hemorrhage and necrotizing enterocolitis.

Regarding the scales to determine clinical fetal wellness, the APGAR score was higher in the neonates of women without pathological prenatal history, which determines the importance of avoiding complications and maintaining adequate prenatal controls. Additionally, we established statistically significant differences with the metabolic state at birth in both study groups. Neonates of women with a pathological prenatal history more frequently presented with metabolic acidosis and hypoxemia, associated with an increase in organic acids concentration because of hypoxia and fetal ischemia secondary to perinatal asphyxia. The same occurs with neonatal homeostasis; neonates of mothers with a pathological prenatal history presented with a higher degree of prematurity and more clinical fetal wellness disturbances associated with a low APGAR score and disruptions in the acid–base balance. There is evidence that the combination of neonatal

https://doi.org/10.1017/thg.2021.12 Published online by Cambridge University Press

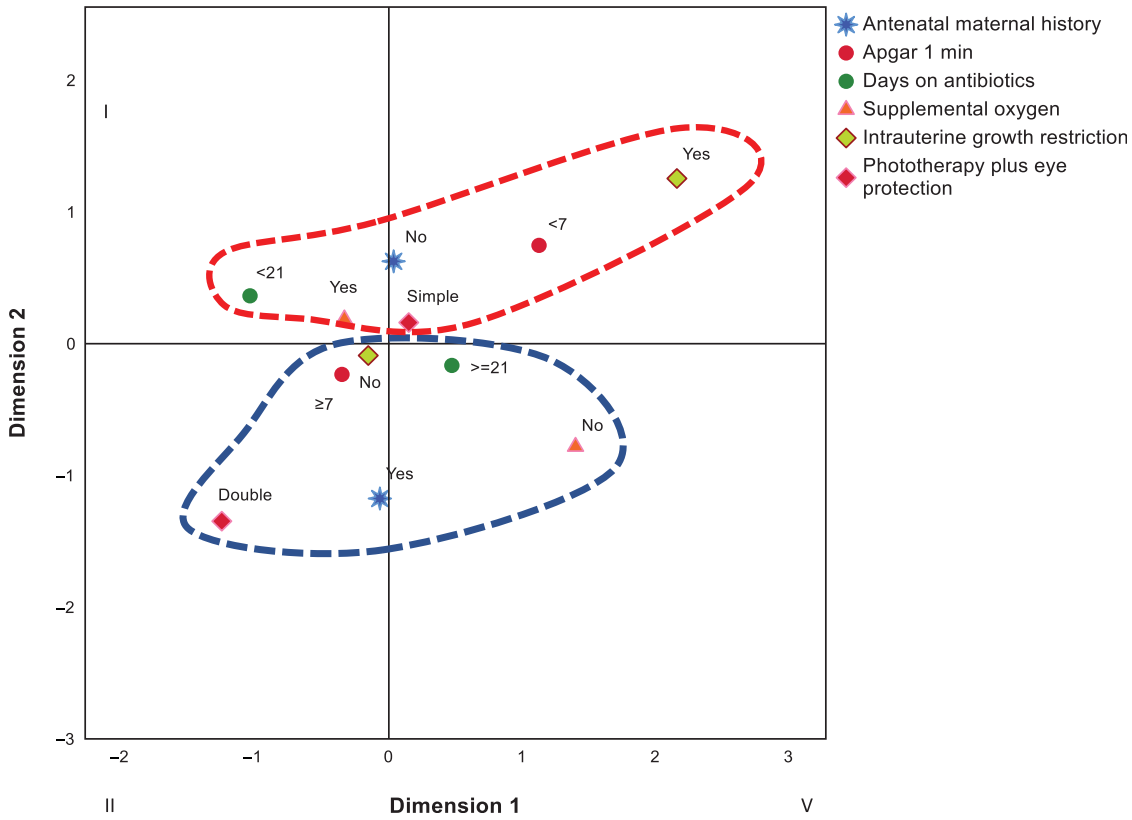

Fig. 1. Multivariate relationship between groups with or without a prenatal maternal history.
Note: Based on categorical principal components multivariate analysis (CATPCA).

acidemia and a low value on the APGAR score in a twin pregnancy are the consequence of alterations in the umbilical cord. These changes can be impingement, torsion or crushing and are due to reduced intrauterine space. It is essential to mention that perinatal asphyxia and newborn sex did not present statistically significant differences related to maternal pathologies in this study. This parameter should be analyzed in a larger population.

Neonates born to women with a relevant maternal medical history frequently require noninvasive mechanical ventilation, double intensive phototherapy and treatment with inotropic and sedative drugs. These factors demonstrate a more severe condition associated with prematurity and other prenatal disorders. The study should be expanded to analyze growth restriction, which in our patients was more frequent in mothers without pathological prenatal history, probably because prematurity limited growth restriction, which occurs in more advanced stages of pregnancy. Likewise, we established significant differences with the persistence of the ductus arteriosus, which was more frequent in neonates of mothers with a pathological prenatal history. These findings are related to acidemia, pulmonary hypertension and respiratory distress in the newborn.

Conclusion

The studied mothers' demographic profile was mostly Mestizos, with a mean age of 32 years, and 93.1% had a poverty status. Most of the twins were diamniotic monochorial and were discordant twins. The study found jaundice, premature anemia and sepsis in 100% of twins and hyaline membrane disease in 89.66% of twins. Twins of women with relevant prenatal care had more premature births (30.4 ± 2.6 weeks), more acid–base imbalance, APGAR at 1 min ≥7 in 90% of cases and patent ductus arteriosus in all. They also required a greater need for double intensive phototherapy than twins of healthy women did.

Acknowledgments. The authors thank Carlos Espinosa, MD, Chief of the Neonatology service at the San Francisco General Hospital, Gonzalo Mantilla MD, Luis Eguiguren MD, and Hugo Burgos PhD, authorities of Universidad San Francisco de Quito.

Financial Support. None.

Conflict of Interest. None.

Ethical Standards. The Human Research Ethics Committee (CEISH) of the San Francisco University of Quito approved this research on November 15, 2019, study code: CA-P2019-159TPG-CEISH-USFQ.

References

Berceanu, C., Mehedințu, C., Berceanu, S., Voicu, N. L., Brătilă, E., Istrate-Ofițeru, A. M., Navolan, D. B., Niculescu, M., Szasz, F. A., Căpitănescu, R. G., & Văduva, C. C. (2018). Morphological and ultrasound findings in multiple pregnancy placentation. *Romanian Journal of Morphology and Embryology*, *59*, 435–453.

Chen, H., Wan, Y., Xi, H., Su, W., Cheng, J., Zhu, C., Lv, J., Wu, X., & Zhao, J. (2019). Obstetric and perinatal outcomes of dizygotic twin pregnancies resulting from in vitro fertilization versus spontaneous conception: A retrospective study. *PeerJ*, *7*, e6638.

Committee on Practice Bulletins–Obstetrics, & Society for Maternal–Fetal Medicine. (2016). Practice Bulletin No. 169: Multifetal gestations: Twin, triplet, and higher-order multifetal pregnancies. *Obstetrics and Gynecology*, *128*, e131–e146.

Esteves-Pereira, A. P., da Cunha, A., Nakamura-Pereira, M., Moreira, M. E., Domingues, R., Viellas, E. F., Leal, M., & Granado Nogueira da Gama, S. (2021). Twin pregnancy and perinatal outcomes: Data from 'Birth in Brazil Study'. *PloS One*, *16*, e0245152.

Ganchimeg, T., Morisaki, N., Vogel, J. P., Cecatti, J. G., Barrett, J., Jayaratne, K., Mittal, S., Ortiz-Panozo, E., Souza, J. P., Crowther, C., Ota, E., Mori, R., & **WHO Multicountry Survey on Maternal and Newborn Health Research Network**. (2014). Mode and timing of twin delivery and perinatal outcomes in low- and middle-income countries: A secondary analysis of the WHO Multicountry Survey on Maternal and Newborn Health. *BJOG*, *121*, 89–100.

Ghi, T., Dall'Asta, A., Franchi, L., Fieni, S., Gaibazzi, N., Siniscalchi, C., Pedrazzi, G., Montaguti, E., Degli Esposti, D., Carpano, M. G., Suprani, A., Orabona, R., Prefumo, F., Vizzardi, E., Bonadei, I., Sciatti, E., Borghi, C., & Frusca, T. (2019). The effect of chorionicity on maternal cardiac adaptation to uncomplicated twin pregnancy: A prospective longitudinal study. *Fetal Diagnosis and Therapy*, *45*, 394–402.

González-Andrade, F. (2020). High altitude as a cause of congenital heart defects: A medical hypothesis rediscovered in Ecuador. *High Altitude Medicine & Biology*, *21*, 126–134.

González-Andrade, F., Sánchez, D., González-Solórzano, J., Gascón, S., & Martínez-Jarreta, B. (2007). Sex-specific genetic admixture of Mestizos, Amerindian Kichwas, and Afro-Ecuadorans from Ecuador. *Human Biology*, *79*, 51–77.

Hviid, K., Malchau, S. S., Pinborg, A., & Nielsen, H. S. (2018). Determinants of monozygotic twinning in ART: A systematic review and a meta-analysis. *Human Reproduction Update*, *24,* 468–483.

Leimberg, M., Martínez, MA., Mendoza, M., Hidalgo, L., & Chedraui, P. (2009). Maternal-perinatal resultant from double pregnancy in the obstetrics hospital Enrique C. Sotomayor. *Revista Medicina*, *15*, 7–13.

Martinka, D., Barrett, J., Mei-Dan, E., Zaltz, A., & Melamed, N. (2019). Respiratory morbidity in late preterm twin infants. *Archives of Gynecology and Obstetrics*, *300*, 337–345.

McLennan, A. S., Gyamfi-Bannerman, C., Ananth, C. V., Wright, J. D., Siddiq, Z., D'Alton, M. E., & Friedman, A. M. (2017). The role of maternal age in twin pregnancy outcomes. *American Journal of Obstetrics and Gynecology*, *217*, 80.e1–80.e8.

Monaghan, C., Kalafat, E., Binder, J., Thilaganathan, B., & Khalil, A. (2019). Prediction of adverse pregnancy outcome in monochorionic diamniotic twin pregnancy complicated by selective fetal growth restriction. *Ultrasound in Obstetrics & Gynecology*, *53*, 200–207.

Monden, C., & Smits, J. (2017). Mortality among twins and singletons in sub-Saharan Africa between 1995 and 2014: A pooled analysis of data from 90 Demographic and Health Surveys in 30 countries. *The Lancet Global Health*, *5*, e673–e679.

Naranjo-Espín, S., & Calle-Miñaca, A. (2015). Evaluation and management of multiple pregnancy in the Obstetric Center of Hospital Carlos Andrade Marín 2012-2014. *La Revista Médica-Científica CAMbios*, *14*, 40–45.

Ndiaye, K., Portillo, E., Ouedraogo, D., Mobley, A., & Babalola, S. (2018). High-risk advanced maternal age and high parity pregnancy: Tackling a neglected need through formative research and action. *Global Health, Science, and Practice*, *6*, 372–383.

Rissanen, A. S., Jernman, R. M., Gissler, M., Nupponen, I., & Nuutila, M. E. (2019a). Maternal complications in twin pregnancies in Finland during 1987-2014: A retrospective study. *BMC Pregnancy and Childbirth, 19*, Article no. 337.

Rissanen, A. S., Jernman, R. M., Gissler, M., Nupponen, I. K., & Nuutila, M. E. (2019b). Perinatal outcomes in Finnish twins: A retrospective study. *BMC Pregnancy and Childbirth*, *20*, Article no. 2.

Sabatelli, D., Milet, B., Mena, P., & Domínguez, A. (2019). Growth restriction increases the risk of bronchopulmonary dysplasia, death, and sepsis in twins of 30 weeks or less of gestation. *Revista Chilena de Pediatria*, *90*, 36–43.

Santana, D. S., Surita, F. G., & Cecatti, J. G. (2018). Multiple pregnancy: Epidemiology and association with maternal and perinatal morbidity. *Brazilian Journal of Gynecology and Obstetrics*, *40*, 554–562.

Santangelo, R., González-Andrade, F., Børsting, C., Torroni, A., Pereira, V., & Morling, N. (2017). Analysis of ancestry informative markers in three main ethnic groups from Ecuador supports a trihybrid origin of Ecuadorians. *Forensic Science International Genetics*, *31*, 29–33.

Smith, L. K., Manktelow, B. N., Draper, E. S., Boyle, E. M., Johnson, S. J., & Field, D. J. (2014). Trends in the incidence and mortality of multiple births by socioeconomic deprivation and maternal age in England: A population-based cohort study. *BMJ Open*, *4*, e004514.

Townsend, R., & Khalil, A. (2018). Fetal growth restriction in twins. Best practice & research. *Clinical Obstetrics & Gynecology*, *49*, 79–88.

Wei, J., Wu, Q. J., Zhang, T. N., Shen, Z. Q., Liu, H., Zheng, D. M., Cui, H., Collaborative Group on Twin Birth and Fetal Abnormality in China**, & Liu, C. X.** (2016). Complications in multiple gestation pregnancy: A cross-sectional study of ten maternal-fetal medicine centers in China. *Oncotarget*, *7*, 30797–30803.

https://doi.org/10.1017/thg.2021.12 Published online by Cambridge University Press