SUPPLEMENTARY MATERIAL

The history of fetal medicine and surgery in Peru gives meaning to the eternity of life

La historia de la medicina y cirugía fetal en el Perú da sentido a la eternidad de la vida

Table. History of Fetal Medicine and Fetal Therapy in Peru

Date	Event	Reference
15000 BC	Humans arrive in South America from Asia	1-4
	The ancient Peruvian physician named *Oquetlupuc*, *hampicamayoc*, *colla camana*, and *yanavilca* knew the properties of native plants such as *Erythroxylum coca* (coca leaves), *Smallanthus sonchifolius* (yacon), *Croton lechleri* (sangre de grado), *Uncaria tomentosa/U. guianensis* (uña de gato), *Lepidium meyenii* (maca), *Physalis peruviana* (golden berry), *Minthostachys mollis* (muña), *Notholaena nivea* (cuti-cuti), *Maytenus macrocarpa* (chuchuhuasi), *Dracontium loretense* (jergon sacha), *Gentianella nitida* (hercampuri), *Plukenetia volubilis* (sacha inchi), *Zea mays* (purple maize), *witapallo*, *chamomile*, *rosemary*, *oregano*, *cedrón*, *queuña*, *llareta*, and other plants. |	6-8
	Quinine is used as an antipyretic	8
	Childbirth is attended by women, eventually becoming midwives	9
	Midwives developed techniques such as body warming and massage, external fetal version, manteo, herbal infusions during delivery, and participation of the father or family members during childbirth. Also included are postpartum and newborn care	10-12
2, 500 BC	Representation of pregnancy and birth at all stages and congenital abnormalities in ceramics	14
400 BC	Cranial trepanation with 40% survival rate	15
1000 BC	Cranial trepanation with 90% survival rate	15
17th Century 1649	Quinine was discovered from the bark of the cinchona tree, *Cinchona officinalis*, native to the Andes and belonging to the *Rubiaceae* family. The Jesuits made the first reports about quinine and cinchona in the book "Sheula Romana".	16
18th Century 1781	Priest Francisco Gonzales Laguna advocated for protocolized childbirth care through "*ZELO SACERDOTAL PARA CON LOS NIÑOS NO NACIDOS*". Chapter VIII discusses cesarean practice in deceased women.	16
	Viceroy Don Agustin de Jauregui issued the decree of September 25, announced by a proclamation on October 10, published as a war decree in Lima's main square, requiring surgeons to perform post-mortem cesareans.	16
1791	Description of a newborn with anencephaly	16
1794	On December 19, a cesarean was performed in Tucumán, Viceroyalty of La Plata, on a mother who died from a lightning strike; the baby was born alive but died minutes later |	16
1797	José Manuel Dávalos graduated from Montpellier Medical School, France, with a thesis titled "Recurrent diseases in Lima and their cure methods", describing pregnancy and childbirth pathologies, infant tetanus, eclampsia, prophylaxis and management of labor, umbilical cord care, colostrum administration, and hygiene rules for newborns	16
1826	October 13, Hipolito Unanue y Pavón, Secretary of Health of Marshal Andrés de Santa Cruz, founded the Maternity House	16
1830	May 12, The Maternity House, under the direction of Benita Paulina Cadeau de Fessel and professors Madame La Chapelle and Antoine Dubois (trained at the Paris School of Midwifery), taught obstetrics	16
1841	Public Benevolent Society of Lima refounded the Maternity House at Santa Ana Hospital	16
1848	Dr. Camilo Segura appointed director of the Maternity House	16
1850	Cocaine was isolated from coca leaves (*Erythroxylum coca*), later leading to the development of local anesthetic lidocaine	8
1851	Cayetano Heredia selected top students and sent them as scholarship recipients to Paris to learn modern medicine and teaching organization	16,18
1853	After specializing in Surgery and Obstetrics in La Soborna, France, Camilo Segura returned to implement techniques for childbirth care	16,18
1856	September 9, the Faculty of Medicine of San Fernando was founded as part of UNMSM, with José Cayetano Heredia Sánchez as its first dean	16,18
1861	First post-mortem cesarean by Camilo Segura	16,18,20,22
1878	June 12, Lino Alarco Bedriñana performed the first ovarian cyst removal (oophorectomy) at the patient's home, using chloroform as anesthesia	32
1885	Samuel Garcia started the "Free Clinic for Pregnant Women" at the Maternity House, the first prenatal care service	16

Date	Event	Reference
1885	October 5, Daniel Alcides Carrión, medical student, died after inoculating himself with blood from a verruca, developing severe acute anemia. His death demonstrated the etiological link between "Fever of La Oroya" and "Peruvian Verruga".	16
1900	May 31, Alberto Barton, medical intern, performed a post-mortem cesarean with a living fetus at Lima's Maternity. The newborn survived.	16,20,22
1910-1936	Cesarean sections performed in Lima, Chiclayo, Arequipa, and Cuzco	16,20.22
1913	First description of "mountain sickness in the Andes," called "puna" in Bolivia and "soroche" in Peru, in foreigners arriving from the coastal city of Antofagasta to work in the mountains up to 5,180 meters above sea level	33
1914	November 9, the first transfusion of citrated blood was performed by Professor Luis Agote García at Rawson Hospital in Argentina	34
1922	October 10, The Maternity House was moved to its current location, officially called the "Obstetric-Gynecological Institute," known as Hospital Maternidad de Lima	16,36
1924	The Archbishop Loayza Hospital was inaugurated with Gynecology services and a Hospitalization Ward (Pavilion V), led by Constantino J. Carvallo Alzamora and assisted by Alfredo Curotto, Luis Esteves, César Heraud, Lucas Molina Navia, Alberto Santos Astete, and Marcelino Castellares	37-39
1927	First scientific medical expedition to the central Andes led by Carlos Monge Medrano, with Alberto Hurtado and three more doctors and eight medical students. Described "Mountain Sickness," "High Altitude Sickness," or "Monge's Disease".	40,41
1937	December 22, Dr. Victor Bazul Fonseca performed the first segmental cesarean	16,20, 22,38
1939	May 14, Lina Medina, age 5, gave birth via cesarean performed by Gerardo Lozada, Alejandro Bussalleu, and Rolando Colareta	16,20,22,38,39
1900-1952	Antonio Lorena Rozas was a leading figure in medicine, anthropology, archaeology, botany, and sociology. Alberto Barton Thompson excelled in microbiology, and Manuel Núñez Butrón in community medicine	42-45
1943	Miguel Aljovín, President of the Peruvian Red Cross, created the first Blood Bank in Peru at the Hospital Dos de Mayo in Lima. In 1944, from that hospital, Carlos Muñoz Baratta began providing blood transfusions in all Lima hospitals using whole blood, washed red blood cells, previously discarded, and employed fresh frozen plasma for the first time	46
1947	The Peruvian Society of Obstetrics and Gynecology was founded under the presidency of Constantino J. Carvallo Alzamora and collaboration of Alfredo Curotto, Luis Esteves, César Heraud C., Lucas Molina Navia, Alberto Santos Astete, and Marcelino Castellares |	16,38,39
1949	First complete exchange transfusion performed in a newborn with hemolytic disease, in collaboration with the blood bank of Hospital Dos de Mayo, on June 19	16,47
1954	Javier Arias Stella reported the endometrial reaction to chorionic hormonal stimulation, confirming it was due to chronic estrogen and progestogen stimulation. The Arias-Stella reaction involves cellular enlargement, especially of the nucleus, up to twice or more the normal size.	48-50
1953-1955	Probable influence of high altitudes on persistent ductus arteriosus in schoolchildren reported	51,52
1956- 1964	Fasting blood glucose levels in pregnant women decreased as they approached term. Later, it was reported that fasting glucose levels in pregnant women are significantly lower than in non-pregnant women	53,54
1958	UNMSM established the first three residency positions in gynecology and obstetrics, obtained by Manuel Alva Saenz, Jose Exebio Adrianzén, and Ramiro Yanque Montufar	55
1956-1983	New faculties of human medicine were established in various universities: Trujillo (Feb 17, 1956), San Agustin de Arequipa (Mar 22, 1958), San Antonio Abad of Cuzco (Aug 25, 1977), San Luis Gonzaga de Ica (Feb 16, 1961), Cayetano Heredia (May 1962), Federico Villarreal (Apr 12, 1966), Piura (1983), and San Martin de Porres (Jul 6, 1983) |	16
1961	First eleven cases of postpartum panhypopituitarism or Sheehan's syndrome reported	56
1961	Inauguration of Hospital Materno-Infantil " San Bartolome"	16
1962-2024	Despite maternal hypoxia at high altitude, fetal oxygenation (umbilical pO2, scalp oxygen tension, fetal oxygen supply) generally remains stable. However, there is a reduction in fetal glucose consumption, umbilical glucose concentration, and blood flow, indicating fetal hypoglycemia. This reduction is more impactful than oxygen deprivation, leading to fetal growth restriction (FGR) and lower birth weight. Hypoglycemia may also decrease fetal insulin levels, inhibiting growth, and increase IGFBP-1 levels, contributing to FGR. Maternal and placental IGFBP-1 levels are elevated under these conditions.	23, 57-72
1962	Introduction of fetal sex diagnosis via chromosomal analysis of amniotic fluid cells	73
1963	William Albert Liley reporta la transfusion peritoneal en fetos con enfermedad hemolitica en Auckland, Nueva Zelandia	74
1964	Abraham Ludmir, Delia Moreno, René Cervantes, and Alfredo Larrañaga, trained in the U.S.A., started Gynecology and Obstetrics specialization at San Fernando Medical School, promoting institutionalized prenatal care by physicians	16
1968	Cayetano Heredia University begins the Medical Residency Program in Gynecology and Obstetrics	16
1970	Until then, no reliable tests existed to assess fetal well-being and lung maturity. The practice of early delivery for diabetic pregnancies based on Priscilla White's management and urinary estriol to prevent fetal death increased perinatal morbidity and mortality due to iatrogenic preterm labor. At Hospital San Bartolome, iatrogenic preterm labor in pregestational diabetes was five times more frequent than in gestational diabetes. However, protocols emphasizing strict glycemic control and fetal biophysical monitoring until lung maturity are now standard, nearly eliminating fetal death and RDS.	75

Date	Event	Reference
1970	Use of continuous positive airway pressure (CPAP) via nasal cannula, neonatal ventilator, and parenteral nutrition	29
1971	The normal labor curve in Peruvian women was reported, defining prolonged labor as >20 hours in nulliparas and >15 hours in multiparas	76
1972	Graham C. Liggins and Robert N. Howie demonstrated that antenatal glucocorticoid use prevented neonatal respiratory distress syndrome in a controlled trial in Auckland. The Cochrane review took 34 years to gather evidence on neonatal corticosteroids; the American College of Obstetricians and Gynecologists recommended it after 44 years	77-79
1973	Radiopelvimetry in 320 pregnant women showed 47% had gynecoid pelvis, 41% platypelloid pelvis , 6% android pelvis , and 6% anthropoid pelvis	80
1975	First description of hormonal variations during the menstrual cycle using the radioimmunoassay method of double antibody	81
1970-1990	First diagnostic laparoscopies and tubal blockages performed at Loayza and Cayetano Heredia Hospitals. From 1990 onward, laparoscopic diagnosis and treatment of various gynecological pathologies expanded	82-91
1977	Elio Quirós, Castro Kikuche, José Quispe, Manuel Mansilla, Honorato Dávila, and Alfredo Guzmán began using ultrasound. Alfredo Guzmán gave the first lecture on intrauterine diagnosis with ultrasound at the Peruvian Society of Obstetrics and Gynecology	16,92
1978-1980	Norbert Freinkel and Boyd Metzger led research on glucose metabolism in normal pregnancy	93.94
1981	The discriminant zone of chorionic gonadotropin levels was described, along with its use in ultrasound evaluation of ectopic pregnancy	95
1986	Ultrasound in prenatal diagnosis of congenital malformations and chorionic villus sampling, amniocentesis for fetal karyotyping were reported	96-98
1988-2016	Juan Denegri, Raul Urquizo, Felix Salgado, Nelly Quinteros, and Gustavo Pinedo formed the first Board of the Peruvian Perinatology Network	16
1992	El hospital Maternidad de Lima was transformed into the "Perinatal Maternal Institute"	16
1989-1990	Fasting blood glucose in pregnancy is maintained between 50-79 mg/dL in the third trimester; values outside are associated with higher obstetric and perinatal morbidity	99
1992	Gestational hyperglycemia is a continuous phenomenon. The best prognosis is when the mean glucose in the Oral Glucose Tolerance Test (OGTT) is <101 mg/dL (mean + 1 SD). Gestational diabetes corresponds to mean + 2 SD	100
1987	INSURE strategy (Intubation, Surfactant, Extubation) with CPAP is less invasive, safer, and reduces mechanical ventilation needs in preterm infants with respiratory distress	29
1988	Although women retain reproductive capacity at high altitude, they experience later menarche and earlier menopause	2,3,101-103
	The book "Prenatal diagnosis of congenital anomalies" was published, becoming an international reference for prenatal diagnosis	104
1989	The need for prophylactic antibiotics in emergency cesarean compared to elective cesarean was reported	105
1953-2016	Congenital anomaly rates are higher at high altitude than at sea level, being four times greater when residing >3500 m above sea level	1,2,51,52, 106,107
1992-2022	One elevated blood glucose value is sufficient to identify women with gestational hyperglycemia in an oral glucose tolerance test (OGTT) who have higher maternal-perinatal complications than normoglycemic women	108-110
1997-2000	Fetal inflammatory syndrome in preterm labor characterized by elevated interleukin-6 in fetal blood was reports. Funisitis and chorionic vasculitis are its histological features.	111-113
2000-2003	The Peruvian Association of Fetal Medicine (APEMEF) was created. Pedro Mascaro Sanchez was the first president. Later, Juan Mere Del Castillo led in 2003, defining the concept of fetal medicine	29
2002	Any pregnant woman with fasting glucose >79 mg/dL before week 36 should undergo a 75g glucose challenge test with measurements at 2 hours, per WHO guidelines. Fasting glucose >79 mg/dL is as effective as postprandial testing for detecting gestational hyperglycemia. Measuring glucose 2 hours after meals reduces detection costs by 59% compared to universal OGTT	114
2000-2012	Compressive suture of the uterus after cesarean delivery for postpartum hemorrhage treatment reduces bleeding and hysterectomy need. The "San Bartolome Technique" is a modification used today	115,116
2007	There is an association between maternal education level, social status, and the severity of child injuries; verbal abuse is most common.	117
	Fetal growth curves for three regions of Peru were published based on data from the Ministry of Health	118
2006-2008	The classification of placental pathological lesions was disseminated, based on the Perinatal Section of the Pediatric Pathology Society (2005), along with current knowledge on placental function	119,120
2008	Living above 2000 m altitude is associated with fetal growth restriction (FGR). There is a gradual decrease of 91 grams in birth weight per 1000 m increase in residence altitude	2,23
2010	Diagnosis and management of fetal anemia were disseminated	121
2005-2014	The utility of 3D and 4D ultrasonography in fetal medicine was promoted	122-124

Date	Event	Reference
2012-2023	Health is the capacity of an individual to maintain balance and adapt across biological, psychological, social, and spiritual dimensions in harmony with their environment. This ability enables individuals to sustain homeostasis, attain inner peace, and engage in mutual social cooperation.	24,25, 125-129
2011	.	130
	Fetos con flujometría Doppler con compromiso hemodinámico severo presentan acidemia y alta tasa alta de mortalidad, independiente del percentil de crecimiento al nacer.	131
	In patients with severe preeclampsia, abnormal cerebral-placental index and irregular Arancio's ductus venosus, as measured by Doppler velocimetry, identified over 65% of newborns with adverse neonatal outcomes and were linked to placental dysfunction (FGR and oligohydramnios).	132
2012-2021	Family history of hypertension and diabetes mellitus is associated with preterm birth, preeclampsia, cesarean section, antenatal hospitalization, and gestational diabetes. Determinants of human health include genetics and environment interactions, influenced by individual, family, community, and societal factors.	24,25, 124-128.133-136
2012	Clinical and ultrasound evidence suggests abnormal fetal-maternal interactions are crucial in pregnancy complications such as FGR, preeclampsia, fetal death, gestational diabetes, and preterm birth.	137
2013	Expectant management of severe preeclampsia before 34 weeks offers no benefit and increases risks of placental abruption and small-for-gestational-age infants	138,139
	Changes in fetal pulmonary artery flow after antenatal corticosteroids, measured by systolic acceleration/deceleration index (TA/TD), reflect fetal lung maturity, with significant differences observed after 33 weeks	140
2014	Termination of pregnancy for medical reasons is a preferable term than "therapeutic abortion"	125
	Decrease in septic abortions causing tubo-ovarian abscesses and increase in pelvic inflammatory disease was reported in Lima	141
2016	Prediabetes during pregnancy can be diagnosed with fasting glucose >75th percentile and <95th percentile after 24-32 weeks using OGTT; associated with higher cesarean risk and larger neonatal size, independent of maternal age, BMI, parity, gestational age, and fetal sex.	109
2017	A table of infant measurements for those born at 3,400 meters above sea level was reported, identifying a higher number of infants at risk of death.	142-145
2018	The prevalence of gestational diabetes is 16% and independently correlates with emotional depression in Lima	136
2020	It is recommended that pregnant women at risk of preeclampsia receive 81 mg/day aspirin from before 16 weeks until delivery for prevention. Expectant management is not recommended for hypertensive disorders in pregnancy ≥34 weeks. Antihypertensive treatment should be initiated within 30–60 minutes in women with systolic BP ≥160 mm Hg and/or diastolic BP ≥110 mm Hg confirmed after 15 minutes or more. Gestational hypertension without proteinuria and other organ failure should be considered severe preeclampsia, and delivery should be induced	146
2022	The Lima Criterion for diagnosing hyperglycemia in pregnancy is based on 659 healthy pregnant women without factors affecting glucose. Hyperglycemia is defined as glucose above the 95th percentile at various times: fasting (>92 mg/dL between weeks 7-36, >88 mg/dL after week 36), 1-hour (>153 mg/dL between weeks 7-32), and 2-hour (>120 mg/dL) throughout pregnancy. This criterion is more sensitive than the IADPSG criteria recommended by FIGO.	110
2022-2023	Telemonitoring via phone calls to pregnant women for prenatal care in settings lacking telemedicine infrastructure is feasible. A complete, personalized prenatal care app was developed using Flutter (version 2.2) for Android and iOS devices	147,148
2024	Plasma soluble fms-like tyrosine kinase 1 to placental growth factor ratio of 11.5 multiples of median predicts preeclampsia with severe features within 2 weeks of testing	149
	Customized growth charts were published for individual fetuses from low-risk pregnancies, and the optimal weight at 40 weeks was calculated using a formula evaluated in 6,598 newborns. The Peruvian personalized charts for middle-class women proved to be reliable for assessing fetal growth, and their detection ability and diagnostic accuracy were similar to other international charts.	150
Fetal Therapy		
Congenital diaphragmatic hernia		
2011	In a 7-year study involving 15 cases without additional anomalies, 33.3% showed intrathoracic herniation of the liver (liver above), with no survivors. Eight cases had a lung-to-head ratio (LHR) greater than 1.2, of which 87.5% survived, whereas in cases with an LHR less than 1.2, only 28.5% survived. The overall mortality rate was 40%, with no fetal deaths, but half of the neonatal deaths were attributed to hypoplasia and pulmonary hypertension, and one was due to post-surgical sepsis. Seventy-five percent (83.3%) of neonatal deaths occurred in fetuses with the liver above, and an LHR greater than 1.2 was a better predictor of survival than the position of the liver.	151
2015	Case of a 39-week primigravida with fetal left diaphragmatic hernia. A fetal EXIT procedure was performed, allowing intubation during delivery and avoiding hypoxia associated with conventional methods. This case demonstrates the potential for successful fetal airway management surgeries.	152
2018	In cases with severe pulmonary hypoplasia, fetoscopic tracheal occlusion increased survival by 30% compared to no intervention. Summarized indications, selection criteria, technique, and outcomes, highlighting differences in neonatal survival rates across Latin America.	153

Date	Event	Reference
2019	Among 380 fetuses with left diaphragmatic hernia in Latin America, 144 without chromosomal or other anomalies had a neonatal survival rate of 31.9%. Survivors had higher O/E-LHR (56.5% vs 34.9%), less hepatic herniation (34.8% vs 80.6%), and higher gestational age at birth (37.8 vs 36.2 weeks). Fetuses with O/E-LHR <35% had only 3.4% survival; 35-45% had 28% with liver up and 50% with liver down; >45% had 50% with liver up and 76.9% with liver down. Indicates high neonatal mortality for CDH. |	154
2022	In Latin America, fetuses with right diaphragmatic hernia without chromosomal or other anomalies with observed -to-expected lung-to-head ratio (O/E-LHR) ≥65% had significantly higher survival than those with O/E-LHR <65% (81.8% vs 15.6%).	155
	Fetoscopic tracheal occlusion with severe or moderate pulmonary hypoplasia was associated with resolution of pulmonary hypertension by age one and at discharge, respectively.	156, 157
Intrapartum ex-utero (EXIT) management for airway obstruction		
2020	Of 235 cases, EXIT therapy was performed at an average of 35.1 weeks. The most common diagnosis was teratoma (46.4%). The most frequent maternal complication was postpartum hemorrhage (4.7%). Fetal or neonatal death occurred in 17%. The most common neonatal issue was failed intubation or tracheostomy (3.4%). EXIT may be considered for oral or cervical tumors with high suspicion of fetal airway obstruction.	158
2020	First two cases of fetal airway obstruction managed with EXIT at third trimester of pregnancy was reported	159
Sacrococcygeal teratoma		
2015	A case at 25 weeks associated with oligohydramnios and fetal demise during hospitalization was reported	160
2016	A 27-week pregnant woman with a giant fetal sacrococcygeal teratoma developed severe anemia. Fetal transfusion prolonged pregnancy and improved perinatal outcome.	161
2025	. A large tumor with rapid growth, a solid component, and high vascularization has a poor prognosis, especially if it causes heart failure due to high cardiac output leading to hydrops and death. The tumor volume to fetal weight ratio (TFR) ≥ 0.12 at 24 weeks is a good predictor of mortality. A new index is proposed that combines the tumor volume in cubic centimeters divided by the fetal head diameter (THC), adding one unit if polyhydramnios is present. A THC combined with polyhydramnios greater than 3.0 identifies all postnatal deaths.	162
Fetal thoracic space-occupying lesions		
2019-2024	Fetal thoracocentesis for severe mediastinal compression and thoraco-amniotic shunting were reported	163-165
Fetal lower urinary tract obstruction		
2024	The use of vesico-amniotic shunts is reported	165,166
Myelomeningocele		
2018	Techniques, evolution, advantages, disadvantages, and future challenges of fetoscopic repair were described.	167
2020	Clinical experience with 314 cases across seven Latin American centers was similar to international reports. Only two centers performed fetoscopic procedures.	168
2021	Neonates with postnatally repaired open neural tube defects had worse motor outcomes than those with prenatal repair. Fetal movement assessment via ultrasound is a useful predictor of postnatal motor function and guides case selection.	169
	Fetal closure of meningomyelocele via fetoscopic approach with uterus exteriorized through two ports was associated with lower risk of neonatal respiratory distress syndrome compared to open hysterotomy.	170
	Fetoscopic repair of open neural tube defects reduces cesarean delivery and preterm birth rates compared to open surgery, with similar total costs, offering a potentially cost-effective option for high-risk pregnancies.	171
2024	Fetal surgery for open neural tube defects with severe ventriculomegaly may not reduce hydrocephalus but helps preserve motor function at 30 months of age	172
	Prenatal repair improves walking ability at 30 months. Lower level of lesion and good motor function predict better outcomes, aiding parental counseling and therapy planning.	173
Renal anomalies and anhydramnios		
2025	Serial amnioinfusion may aid initial survival in bilateral renal agenesis but does not prevent postnatal comorbidities. Further research is needed before routine use. Additional studies are needed for long-term benefits of vesico-amniotic shunts or fetal cystoscopy in lower urinary tract obstruction.	174
Placenta, umbilical cord and fetal membranes		
Monochorionic pregnancy complications		
	Twin-to-twin transfusion syndrome	175-181
	Inverted arterial perfusion sequence and other discordant anomalies	182-184
	Anemia-polycythemia sequence in twins	185,187
	Selective intrauterine growth restriction	186,187
	Amniotic band syndrome	188,189
	Chorioangioma	190
	Fetal anemia	121,191

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