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Physical capability in a rural birth cohort at the age of 52: association with early environmental, nutritional, and developmental factors

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Abstract

Introduction: Midlife physical capability (PC) is associated with developmental factors in the populations of economically developed countries. As far as we know, there is no information for rural populations of low- and middle-income countries. The aim of the study was to investigate the influence of pre- and postnatal factors on midlife objective measures of PC in a 1966–67 birth cohort from a Mexican rural community. The hypothesis was that adverse developmental conditions are associated with low midlife PC.

Methods: In 1966–67, a birth cohort of all children from a poor Mexican rural community was assembled. Data on family socioeconomic status (SES), parental health and nutritional status, birth weight, postnatal growth and feeding patterns were registered. In 2018, out of the 336 cohort members, 118 were living in the community, and eighty-two of them underwent a comprehensive clinical evaluation. The evaluation included grip strength, gait velocity and chair-stand PC tests. In multivariable linear models, PC tests were the dependent variables, and prenatal, birth and postnatal factors were the independent variables. Adjustment for confounding was made with adult anthropometric, body composition, clinical and ageing status variables.

Results: Independent of adult health status and other ageing indicators, lower PC was associated with family organization and SES, parental nutritional status, birth weight, infant postnatal growth velocity, and weaning time. These results indicate that adverse family and environmental conditions that are prevalent in poor rural communities are associated with low midlife PC.

Keywords: Developmental origins, Maternal malnutrition, Infant malnutrition, Adult physical capability, Accelerated ageing

Introduction

Several investigations have confirmed that exposure to adverse environmental conditions during periods of growth and development is related to adult chronic pathological conditions and age-associated diseases. One of the main identified factors is maternal undernutrition [1]. This association has been explained by the concept of "developmental programming by early-life

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undernutrition" [2]. The evidence of this relationship comes from studies of populations exposed to prenatal famine episodes and adult health outcomes [3, 4]. However, poor rural communities of low-income and middle-income countries present a different nutritional epidemiological pattern characterized by chronic protein energy maternal and infant undernutrition [5]. Long-standing cohort studies in these types of communities have confirmed the association of maternal and child undernutrition with adult outcomes such as height, education level, income level, birth weight of offspring, BMI, glucose concentration, and blood pressure [6].

We lack knowledge of the association of adverse developmental conditions of subjects born in poor rural communities and the level of physical capability in adulthood. In economically developed countries, it has been found that prenatal and childhood growth are associated with the level of physical capability [7]. The hypothesis of the study was that adverse early developmental conditions accelerate the loss of physical capability in adulthood. Thus, the aim of the study was to assess the physical capability of members of a birth cohort of all children born in a poor rural community of Mexico in 1966–67 and its association with early developmental conditions.

Methods

The initial study

The study used data from the Tlaltizapán Birth Cohort, which consisted of all born -336 children- in the rural community of Tlaltizapán, in the State of Morelos, Mexico, between March 1st, 1966, and February 28th, 1967. The objective of that study was to investigate the impact of childhood malnutrition on growth and mental development [8]. All pregnant women in the community were identified, and data on the household physical and sanitary conditions, and the parents' height, weight, personal hygiene, formal education, income, and access to mass media were registered. At delivery, the health status and anthropometric measurements of the infant were obtained. The children's physical and mental development were followed for approximately 14 years [9–12].

The present study

At the time of the death of the principal investigator in 1998, [13] most of the research files were lost. Twenty years later, we were able to recover information that allowed us to trace the members of the birth cohort and investigate their status. We found that four members died in utero, 22 died in the 1st year (death rate of 65.5/1000 LB) and 6 died before five years (death rate of 17.8/1000 people). It was not possible to locate 133 of the subjects (39.6%); from the remaining subjects, 10 (3.0%) lived in other Mexican States, and 43 (12.8%) lived in the USA.

We contacted 118 subjects (35.1%) still living in the community; eighty-two of them (50 women and 32 men), aged 51–52 years, agreed to participate in the study and gave written informed consent to be clinically evaluated. We recovered original information on the household's sanitary level, family organization, size, and SES, the anthropometric data of both parents, and the mother's reproductive history. Data on infant birth weight was recovered in 21% of the cases, increments of weight, height, and head circumference in the first six months were recovered in 56.1% of the cases and weaning age was recovered in 46% of the cases.

The clinical evaluation took place at the National Institute of Geriatrics, Mexico City (INGER) between August 2018 and March 2019. The following parameters were evaluated: 1. Anthropometric data: weight, height, arm, waist, and calf circumferences; 2. Body composition: a) Lean, bone and fat mass measured with dual X-ray absorptiometry [DEXA, (*HOLOGIC[®], Discovery QDR Series[®]), [14] and b) muscular and fat mass with bioimpedance (seca MBCA 514n) [15]; 3. Geriatric syndromes using the a) Cognitive Scale (Mini mental state examination, MMSE[®]), [16] b) Depression Scale, (CESD-7), [17] c) Risk and Fear of Falls Scales, [18, 19] d) Drug Consumption Scale, [20] e) Fried Frailty Scale, [21] f) Barthel and Lawton Functionality and Daily Life Activities scale, [22, 23] and g) Champ's Physical Activity and Energy Consumption assessment; [24] 4. PC evaluation: a) Hand Grip Strength (HGS) (Handgrip Dynamometer[®] with duplicate measurements for each hand, with the subjects in a standing position with the elbow at an angle of 180 degrees, and highest measurement was taken as the final value), [25] b) Gait Speed (GS) (Walkway measuring equipment (Gaitrite[®] Mod. Platinum 20), [26] c) the 30-s Chair Stand Test (ChS) (Silverfit[®]), [27] and d) the Standing Balance- Eyes Opened Test (SB) comprised tandem, semitandem, side-by-side stands, and one-legged balance; [28] 5. Self-reported smoking status and alcohol intake, and chronic morbidities; [29] 6. History of heart attack, stroke, cancer, diabetes mellitus, and arterial hypertension; 7. Sitting and standing blood pressure, pulse and respiratory rates, and oxygen saturation were measured in duplicate and with standardized measurements; 8. Biochemical, chemical, and haematological measurements of 36 analytes performed with standardized automatic equipment; and 9. Diagnoses of obesity, osteoporosis, diabetes mellitus, dyslipidaemias, hypertension, and anaemia, with international criteria adapted to the Mexican population. All evaluations were made by standardized professional nurses with the subjects wearing light clothing.

All participants provided written informed consent for the study, genetic data and personal information security.

Enrolment and consent procedures for this study were approved by the institutional review boards of the Bioethics and Research of the National Institute of Geriatrics and of the National Institute of Paediatrics under the number INP-INGER 06/2018. All methods employed in the study were performed in accordance with the relevant international guidelines and regulations, as well as those from the Ley General de Salud of Mexico.

Statistical analysis

We used multiple linear regression in R software (R 3.4.3, Vienna, Austria: R Foundation for Statistical Computing) [30]. The first step of model building aimed to identify the adult clinical variables significantly associated with HGS, GS, ChS scores, and SB scores. Since the SB scores showed low variability, they were eliminated from further analysis. In the second step of the analysis, to control for confounding factors, we built a model for each prenatal, birth and postnatal infant variable, adjusting for adult

variables that proved to be significantly associated with the PC variables.

Results

Table 1 presents the descriptive statistics of the anthropometric, clinical, functional and pathological variables of the participants aged 51–52 years that showed statistical significance in the multivariable models.

Both men and women had near low median height, with low minimum values, and median BMI in the normal range. The median HGS of women was very low; the prevalence of diabetes mellitus and systemic arterial hypertension were high, and there was a deficit in the MMSE test.

Table 2 shows the descriptive statistics of the prenatal, birth, and postnatal variables of the participants, their parents, and family.

The described variables were those with a significant association with PC outcome variables in the multivariable models. At the participants’ births, the families were

Table 1 Participants’ somatometric, clinical, functional, and pathological characteristics measured at age 51–52 by sex

| Variable | Women (N=50) | | | Men (N=32) | | |
|---|--------------|----------|---------|------------|----------|---------|
| | Median | Min | Max | Median | Min | Max |
| Quantitative variables | | | | | | |
| Adult height (m) | 1.54 | 1.40 | 1.62 | 1.65 | 1.53 | 1.82 |
| Right Leg Length (cm) | 82.0 | 71.0 | 87.6 | 84.6 | 73.0 | 96.2 |
| Knee height (cm) | 42.9 | 37.0 | 50.5 | 46.8 | 40.3 | 51.0 |
| Foot width (cm) | 9.0 | 8.0 | 10.5 | 10.0 | 9.0 | 11.0 |
| Body Mass Index (kg/m ²) | 29.8 | 20.8 | 42.1 | 27.8 | 21.5 | 39.6 |
| Lean mass index (muscular kg/m ²) | 15.55 | 12.30 | 19.30 | 18.45 | 14.90 | 22.70 |
| Energy expenditure (kcal/day) | 2,055.3 | 1,781.7 | 2,626.4 | 2,938.60 | 2,503.8 | 4,031.5 |
| Bioelectric impedance phase angle (°) | 5.3 | 3.4 | 6.4 | 5.8 | 4.8 | 6.6 |
| Resting respiratory rate (breaths/minute) | 18 | 15 | 24 | 20 | 14 | 25 |
| Resting Diastolic Blood Pressure (mmHg) | 70 | 50 | 98 | 77 | 60 | 96 |
| Pulse pressure (mmHg) | 40 | 25 | 80 | 40 | 24 | 68 |
| Uric acid blood concentration (mg/dl) | 4.8 | 3.0 | 8.2 | 6.2 | 4.1 | 9.0 |
| Depression Score | 5 | 0 | 19 | 1 | 0 | 12 |
| Frailty index | 1 | 0 | 4 | 1 | 1 | 3 |
| Grip strength (kg) | 22 | 12 | 32 | 40 | 21 | 52 |
| Gait speed (cm/s) | 105.8 | 66.1 | 157.9 | 107.7 | 79.3 | 152.9 |
| Chair stand test (stands/30 s) | 16 | 12 | 21 | 17 | 12 | 26 |
| Bipodal balance (s) | 10 | 10 | 10 | 10 | 10 | 10 |
| Semitandem balance (s) | 10 | 10 | 10 | 10 | 10 | 10 |
| Tandem balance | 10 | 7 | 10 | 10 | 10 | 10 |
| One-legged balance | 10 | 0 | 10 | 10 | 9 | 10 |
| | Women | | | Men | | |
| Dichotomous variables | n | % | | n | % | |
| Type 2 diabetes mellitus | 10 | 20% | | 5 | 16% | |
| Systemic arterial hypertension | 11 | 22% | | 7 | 22% | |
| Mini-Mental State Examination (deficit defined by Folstein criterion) | 5 | 10% | | 4 | 13% | |

Table 2 Characteristics of the prenatal, birth and postnatal variables of the participants, their parents, and their family

| Quantitative variables | Women | | | | Men | | | |
|---|-----------------------------|--------|-------|-------|-------|--------|-------|------|
| | N | Median | Min | Max | N | Median | Min | Max |
| Participant's Z score of weight for age at birth | 17 | -0.68 | -2.25 | 1.26 | 12 | -0.69 | -1.32 | 1.15 |
| Participant's Z score of head circumference at birth | 4 | -0.53 | -0.75 | -0.32 | 6 | 0.42 | -1.15 | 1.21 |
| Participant's increase in arm circumference from the 3rd to 4th month (cm) | 46 | 0.6 | -1.3 | 2.0 | 29 | 0.5 | -0.9 | 2.0 |
| Participant's weaning age (months) | 38 | 16.5 | 2 | 28 | 23 | 15 | 1 | 23 |
| Postpartum maternal BMI (kg/m ²) | 48 | 23.1 | 18.0 | 31.1 | 32 | 23.9 | 19.4 | 36.6 |
| Father's BMI (kg/m ²) | 45 | 21.9 | 18.7 | 31.7 | 31 | 21.8 | 14.7 | 29.5 |
| Father's formal education (years) | 46 | 2 | 0 | 16 | 31 | 2 | 0 | 11 |
| Number of family members at birth | 47 | 7 | 3 | 13 | 32 | 5 | 3 | 13 |
| Family SES (The higher the value, the lower the status) | 45 | 14 | 5 | 19 | 28 | 13 | 7 | 20 |
| Ordinal/Dichotomous variables | Women | | Men | | Women | | Men | |
| | n | % | n | % | n | % | n | % |
| Participant's Z score of weight increase from birth to 6 months | <-1 | 19 | 41.3% | 10 | 34.5% | | | |
| | -1 to +1 | 20 | 43.5% | 15 | 51.7% | | | |
| | >+1 | 7 | 15.2% | 4 | 13.8% | | | |
| Participant's Z score of head circumference increase from birth to 6 months | <-2 | 6 | 13.0% | 3 | 10.3% | | | |
| | -2 to +1 | 37 | 80.4% | 16 | 55.2% | | | |
| | >+1 | 3 | 6.5% | 10 | 34.5% | | | |
| Mother's height Z score | <-1.5 | 39 | 81.3% | 26 | 81.3% | | | |
| | -1.5 to 0 | 9 | 18.7% | 5 | 15.6% | | | |
| | >0 | 0 | 0% | 1 | 3.1% | | | |
| Mother's postpartum BMI | <19 kg/m ² | 1 | 2.1% | 0 | 0% | | | |
| | 19 to <25 kg/m ² | 35 | 72.9% | 20 | 62.5% | | | |
| | ≥25 kg/m ² | 12 | 25.0% | 12 | 37.5% | | | |
| | | | | | | | | |
| Father's BMI | <19 kg/m ² | 1 | 2% | 2 | 6% | | | |
| | 19 to <25 kg/m ² | 36 | 80% | 25 | 81% | | | |
| | ≥25 kg/m ² | 8 | 18% | 4 | 16% | | | |
| | | | | | | | | |
| Family's SES | High | 10 | 22.2% | 6 | 21.4% | | | |
| | Middle | 21 | 46.7% | 15 | 53.6% | | | |
| | Low | 14 | 31.1% | 7 | 25.0% | | | |
| Family type | Nuclear | 41 | 85.4% | 23 | 90.6% | | | |
| | Extended | 7 | 14.6% | 9 | 9.4% | | | |

large, with a low to middle SES, and a father with a low level of formal education. The median paternal BMI fell within the normal range; based on a postpartum weight measurement, the median maternal BMI presented a distribution from a low (18.0) to a relatively high value (31.1), with a median within the normal range. The categorical mothers' height distribution showed that they were of short stature compared to the international standard. The median Z score values of birth weight, head circumference, and the increments during the first six months of life showed distributions skewed to low values relative to the international standards [31, 32].

Table 3 presents the HGS, GS and ChS predictors of adult age in the multivariable model.

Related to HGS, male sex, height, lean mass, and phase angle (bioimpedance indicator of muscular mass) had significant positive effects, while energy expenditure and pulse pressure had negative effects; the depression score

showed a trend towards significance with a negative effect. Regarding GS, foot width, resting respiratory rate, diastolic blood pressure, uric acid blood concentration, and the diagnosis of diabetes mellitus showed a positive association. Variables negatively associated with GS were male sex, BMI, leg length, knee height, the diagnosis of hypertension and poor performance on the MMSE. With the ChS test, male sex was the only variable that was positively associated, while height and the frailty index variables were negatively associated.

Table 4 shows the prenatal, birth and postnatal variables with significant effects on HGS, GS, and ChS scores, each of which was adjusted by the adult predictors described in Table 3.

The higher the body size at birth (birth weight, birth head circumference), family SES, parental nutrition (maternal and paternal BMI), and family size, the higher the adult maximal HGS. Infant growth measurements in

Table 3 Hand grip strength (HGS), gait speed (GS) and chair stand test (ChS) adulthood predictors

| Dependent | Predictor | Coefficient (95% CI) | P | Adjustedr2 | Globalp-value |
|-------------------|---|--------------------------|----------|------------|---------------|
| HGS (kg) | (Intercept) | -93.06 (-116.5 to -69.6) | < 0.001 | 0.8794 | < 0.001 |
| | Sex (Female 1, Male 2) | 7.93 (4.64 to 11.21) | < 0.001 | | |
| | Adult height (m) | 64.33 (49.69 to 78.96) | < 0.001 | | |
| | Lean mass index (muscular kg/m ²) | 0.83 (0.26 to 1.39) | 0.0046 | | |
| | Energy expenditure (kcal/day) | -0.01 (-0.01 to -0.001) | 0.0092 | | |
| | Bioelectric impedance phase angle (°) | 2.13 (0.54 to 3.72) | 0.0094 | | |
| | Pulse pressure (mmHg) | -0.1 (-0.18 to -0.02) | 0.0207 | | |
| | Depression Score | -0.15 (-0.3 to < 0.0001) | 0.0501 | | |
| GS (cm/s) | (Intercept) | 212.7 (127.29 to 298.12) | < 0.001 | 0.462 | < 0.0001 |
| | Sex (Female 1, Male 2) | -22.05 (-35.51 to -8.58) | 0.002 | | |
| | Body Mass Index (kg/m ²) | -2.08 (-2.91 to -1.26) | < 0.001 | | |
| | Grip strength (kg) | 1.32 (0.69 to 1.96) | < 0.001 | | |
| | Right Leg Length (cm) | -1.78 (-2.76 to -0.79) | < 0.001 | | |
| | Knee height (cm) | -1.56 (-2.89 to -0.24) | 0.021 | | |
| | Foot width (cm) | 7.17 (0.9 to 13.43) | 0.026 | | |
| | Resting respiratory rate (breaths/minute) | 1.78 (0.47 to 3.08) | 0.008 | | |
| | Resting Diastolic Blood Pressure (mmHg) | 0.56 (0.17 to 0.96) | 0.006 | | |
| | Uric acid blood concentration (mg/dl) | 4.31 (1.79 to 6.82) | 0.001 | | |
| | Type 2 Diabetes mellitus (with diagnosis = 1) | 11.1 (2.48 to 19.71) | 0.012 | | |
| | Systemic Arterial Hypertension (with diagnosis = 1) | -9.85 (-18.26 to -1.44) | 0.022 | | |
| | Mini-Mental State Examination (Normal = 0, Deficit = 1) | -11.19 (-21.19 to -1.19) | 0.029 | | |
| ChS (stands/30 s) | (Intercept) | 38.56 (22.74 to 54.38) | < 0.0001 | 0.1342 | 0.0027 |
| | Sex (Female 1, Male 2) | 3.18 (1.39 to 4.96) | 0.0007 | | |
| | Adult height (m) | -15.82 (-26.59 to -5.05) | 0.0045 | | |
| | Frailty index | -1.14 (-2.02 to -0.26) | 0.0111 | | |

the first six months were negatively associated with HGS; higher increment values of weight and head circumference, standardized for age and sex, were negatively associated with HGS; increases in arm circumference from the 3rd to 4th months of age also had a negative effect. Performance on the GS test was negatively affected by maternal size (high and low BMI, and low and above-median height), low family SES, living in a nuclear family at birth and both slow and accelerated head circumference growth. Having been weaned later and having a father with more formal education were variables that were associated with better performance on the test. For the ChS test, having a long weaning period was the only variable found to be significantly and negatively associated.

Discussion

The specificity and strength of the associations of the PC tests with early influences found in the present study can be derived from the set of adjustment variables associated with each of them, i.e., for HGS, the main predictive variables were adjusted by sex, height, and muscular

mass; for GS, they included sex and body shape variables, such as leg length, foot width, and BMI; and in the ChS model, the only variables were sex, height and the frailty index. These differences in adjustment variables by test indicate the different physiological parameters required to adjust in modelling the environmental and developmental associations.

Our results confirm the association of prenatal and birth factors with midlife PC in adults. These results are consistent with the hypothesis of the developmental origins of adult health and disease [2, 33, 34]. The negative association of HGS with weight and head circumference increments during the first six months of life that was found provides new insight into early life adverse influences on adult PC in a group of underprivileged subjects with a rural background. In the case of populations of European ancestry, the Northern Finland Birth Cohort Study, an investigation on growth during the first year of life, reported that greater infant weight gain was associated with lower muscle endurance and poorer aerobic fitness in adulthood, although these effects could have been mediated by adult body size [35]. In our case, the

Table 4 Effects of prenatal and childhood variables on physical capability tests adjusted by adulthood variables

| Variable | Coefficient (95% CI) | P | Adulthood variables included in the model | AdjustedR2 | N |
|---|-------------------------------------|---------|---|------------|----|
| Grip strength (kg) | 4.5 (0.6 to 8.4) | 0.027 | Phase angle, Depression score | 0.4633 | 29 |
| Z score of weight for age at birth (S.D.) | 2.14 (0.77 to 3.51) | 0.012 | Sex, energy expenditure, pulse pressure, depression score | 0.9916 | 10 |
| Z score of head circumference at birth (S.D.) | -0.44 (-0.75 to -0.14) | 0.005 | Sex, lean mass index, pulse pressure | 0.7894 | 72 |
| Prenatal family SES (The higher the value, the lower the status) | 0.27 (0.01 to 0.53) | 0.040 | Sex, adult height, energy expenditure, phase angle, depression score | 0.8688 | 79 |
| Post-gestational maternal BMI (kg/m ²) | 0.31 (0.01 to 0.62) | 0.040 | Sex, adult height, lean mass index, pulse pressure, energy expenditure | 0.8673 | 75 |
| Prenatal paternal BMI at birth (kg/m ²) | 0.67 (0.34 to 0.99) | < 0.001 | Sex, adult height, lean mass index, pulse pressure, energy expenditure | 0.8899 | 78 |
| Number of family members at birth | -1.17 (-2.24 to -0.1) | 0.033 | Sex, height, lean mass index, depression score, pulse pressure, energy expenditure | 0.8749 | 74 |
| Increase in arm circumference from 3rd to 4th month (cm) | -1.67 (-3.49 to 1.49) | 0.071 | Sex, height, lean mass index, energy expenditure, phase angle, pulse pressure, depression score | 0.8867 | 74 |
| Z score of weight increase from birth to 6 months | > +1 Z (vs < -1 Z) | 0.037 | Sex, height, lean mass index, energy expenditure, phase angle, pulse pressure, depression score | 0.893 | 74 |
| Z score of head circumference increase from birth to 6 months | < -2 Z (vs -2 Z to +1 Z) | 0.625 | Sex, height, lean mass index, energy expenditure, angle phase, pulse pressure, depression score | 0.2906 | 80 |
| Z score of head circumference increase from birth to 6 months | > +1 Z (vs -2 Z to +1 Z) | 0.003 | Right leg length, foot width, BMI, diabetes mellitus, MMSE result, blood uric acid | 0.4958 | 61 |
| Living in a nuclear (vs extended) family at birth | -11.06 (-21.75 to -0.37) | 0.0427 | Sex, right leg length, knee height, BMI, grip strength, blood uric acid, resting diastolic blood pressure, resting respiratory rate | 0.4902 | 76 |
| Weaning age (months) | 0.55 (0.02 to 1.07) | 0.0423 | Sex, right leg length, foot width, BMI, grip strength, resting diastolic blood pressure, blood uric acid, diabetes mellitus, MMSE | 0.3968 | 79 |
| Prenatal father's education level (years) | 1.5 (0.43 to 2.57) | 0.0067 | Right leg length, knee height, grip strength, BMI, diabetes mellitus, blood uric acid | 0.4331 | 72 |
| Post-gestational Mother's BMI | -32.86 (-62.43 to -3.28) | 0.0300 | Sex, right leg length, knee height, foot width, grip strength, resting diastolic blood pressure, blood uric acid, diabetes mellitus, MMSE | 0.3415 | 79 |
| Post-gestational Mother's BMI | ≥ 25 kg/m ² (vs normal) | 0.0193 | Right leg length, knee height, grip strength, BMI, diabetes mellitus, blood uric acid | 0.3252 | 75 |
| Prenatal family's socioeconomic status | -8.64 (-15.84 to -1.44) | 0.0193 | Sex, right leg length, knee height, foot width, grip strength, BMI, resting diastolic blood pressure, resting respiratory rate | 0.2721 | 61 |
| Prenatal family's socioeconomic status | Medium (vs High) | 0.4786 | Sex, right leg length, knee height, foot width, grip strength, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Prenatal family's socioeconomic status | Low (vs High) | 0.0231 | Sex, right leg length, knee height, foot width, grip strength, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Prenatal Mother's Height Z score | -11.83 (-21.97 to -1.68) | 0.0035 | Right leg length, grip strength, BMI, diabetes mellitus | | |
| Prenatal Mother's Height Z score | < -1.5 Z score (vs ≥ -1.5 to < 0 Z) | 0.0493 | Right leg length, foot width, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Prenatal Mother's Height Z score | ≥ 0 Z score (vs ≥ -1.5 to < 0 Z) | 0.0493 | Sex, adult height, frailty index | | |
| Head circumference growth velocity from 0 to 6 months age (Z score) | -16.75 (-27.32 to -6.18) | 0.0023 | Right leg length, foot width, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Head circumference growth velocity from 0 to 6 months age (Z score) | < -2 Z score (vs -2 to < +1 Z) | 0.0058 | Right leg length, foot width, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Head circumference growth velocity from 0 to 6 months age (Z score) | ≥ +1 Z score (vs -2 to < +1 Z) | 0.0058 | Right leg length, foot width, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Chair stand test (stands/30 s) | -13.5 (-22.96 to -4.05) | 0.0058 | Right leg length, foot width, BMI, resting diastolic blood pressure, resting respiratory rate | | |
| Weaning age (months) | -0.12 (-0.21 to -0.03) | 0.0110 | Sex, adult height, frailty index | | |

* Every childhood variable coefficient corresponds to a single and different multivariable model

adjustment variables included height and muscle mass. Other studies in economically developed populations have shown that unfavourable influences such as low SES, maternal education and income experienced during prenatal and childhood periods were associated with weaker HGS, low muscular strength, or worst PC in adulthood [33, 36–40]. There are also reports of positive effects of birth weight on muscle strength both in association with or independent of body size [41–43].

In our study, the associations of environmental, prenatal, birth and postnatal factors with midlife PC tests were positive or negative. For instance, better midlife HGS performance was positively associated with family SES and size, maternal and paternal nutritional status, and birth weight. These results suggest that the prenatal improvement of these parameters could result in better future ageing trajectories and adult PC performance. On the negative side of the spectrum, postnatal growth velocity indicators showed a negative association with HGS, a result that is consistent with the high incidence of postnatal malnutrition due to diarrhoeal diseases and the late introduction of foods that are different from the mother's milk, a pattern commonly found in Tlaltizapán [11, 12]. In the same way, in a Finnish cohort study, BMI increases from ages 2 to 11 years in males (but not in females) was positively associated with frailty at 67–79 years of age [44]. In contrast, in a British cohort, height increases, from ages 2 to 7 years, was also related to HGS but with a positive effect [42]. Regarding GS, better performance was associated with higher levels of the father's formal education, which is an SES indicator. This result is consistent with a Chinese study that reported that an illiterate paternal education level (vs. literate) in early life was associated with an increased risk of frailty at ≥ 60 years of age [45]. Infant feeding habits have been associated with the development of malnutrition in rural populations. In the present study, better GS performance was associated with late weaning, a probable nutritional protective factor in a poor rural environment; the median weaning age of the participants was 15 and 16 months for men and women, respectively, with a range of 1 to 28 months. Sanjur, Cravioto, and coworkers reported the practice of prolonged breastfeeding among the cohort's mothers [46, 47]. Similarly, the early introduction of foods that were different from breast milk was a risk factor for marasmus because of the deficit of high-quality protein and energy. As was the case for HGS, postnatal growth velocity indicators were negatively associated with GS performance, confirming the influence of postnatal malnutrition on midlife PC. In addition, lower GS performance was associated with social factors such as family type and SES. To interpret these findings, it can be speculated that poor nuclear rural families

lack sufficient support from other family members. This hypothesis is consistent with other studies where low SES in childhood or before the age of 16 was associated with low GS in adulthood [37, 48]. Indicators of maternal nutritional level (post-gestational BMI and height) were negatively associated with GS performance. Height is considered a cumulative index of nutrition, [49] and the cohort's mothers were of short stature; Cravioto et al. reported that the median height of the cohort's mothers was 147.5 cm, and the first quartile was only 145.5 cm [8], a short stature compared with international standards. The multivariable model for the ChS test showed only a weak negative association with weaning age, a result that contrasts with studies that reported the influence of social variables such as the father's occupational class and low SES on ChS performance [33, 50].

Overall, our results indicate the negative influence of a poor rural family environment, a low nutritional status of parents, especially of the mother, and low intrauterine and postnatal growth, the latter associated with inadequate infant feeding practices, on midlife PC. At the time of the cohort's inception, the relatively small Mexican rural community of Tlaltizapán had a low standard of living, as documented by Cravioto et al. in the Monograph [8]. The health and nutrition surveys at that time revealed that extended families lived in households with poor sanitary conditions and consumed a monotonous diet limited in energy and high-quality protein. Thus, early deficient nutritional status is most likely a contributing factor to the low average HGS of the participants, compared with the average of adults of the same age of economically developed countries and even of residents of Mexico City, as shown in Table 5 [25, 51–53]. This observation is consistent with the report by Dodds et al. [54], who showed that normative HGS data from developing regions were lower than those of developed regions of the world.

Muscular strength, an important component of PC, particularly HGS, is a function of muscle mass development during the foetal stage. In a Finnish study of elderly frail women, postpartum maternal BMI was related to muscle strength in specific (but not in most) muscle groups: the daughters of obese mothers were weaker than the daughters of lean mothers [57]. On the other side of the nutritional spectrum, it has been demonstrated that maternal undernutrition limits the proliferation of precursor muscular cells and reduces the number of fibres formed, a process thought to be mediated by epigenetic changes that could explain, among other factors, the lasting effects on midlife PC [56, 58]. At the time the original research was implemented in Tlaltizapán, nearly 70% of the Mexican population lived in rural communities of similar conditions,

Table 5 Handgrip strength by sex in our study and four community studies with a similar age group

| Sex | Source | Age range | N | Mean | 95%CI | Significance* |
|---------|------------------|-----------|------|------|-----------|---------------|
| Females | Current study | 51--52 | 50 | 22.2 | 20.9—23.5 | Lowest |
| | Mexico City [28] | 50 – 59 | 75 | 25.0 | 24.1—25.9 | 2nd Lowest |
| | Korea [54] | 50 – 54 | 535 | 26.9 | 26.5—27.3 | |
| | USA [55] | 50 – 59 | 780 | 27.5 | 27.1—27.9 | |
| | UK [56] | 51 – 55 | 4250 | 27.5 | 27.3—27.7 | |
| Males | Current study | 51--52 | 32 | 38.5 | 36.1—40.9 | Lowest |
| | Mexico City [28] | 50 – 59 | 74 | 42.0 | 40.9—43.1 | |
| | Korea [54] | 50 – 54 | 386 | 43.3 | 42.7—43.9 | |
| | USA [55] | 50 – 59 | 721 | 42.1 | 41.5—42.7 | |
| | UK [56] | 51 – 55 | 3743 | 46.2 | 45.9—46.5 | Highest |

* Significant difference if 95%CI of one group does not imbricate with 95%CI of another

which favoured the incidence and prevalence of malnutrition. The extensive rural–urban migration that has taken place in Mexico in recent decades has reversed that proportion. The present urban population faces a high prevalence of obesity, diabetes, and hypertension. Demographic transitions in low-income countries has been characterized by four intergenerational cycles [57]. In our study, we documented low nutritional status in at least three generations: the cohort's grandmothers (data not shown), and stunted mothers giving birth to undernourished children who, in midlife, suffer from chronic conditions such as obesity, diabetes and hypertension.

The loss of information from the original study and the reduced sample size, partially due to refusal of the clinical evaluation, are the main limitations of the study. However, our study, although on a limited scale, contributes to the understanding of the present health problems and future ageing trajectories that populations, such as the Mexican population, are likely to face in the future.

Conclusions

The midlife physical capability of adults born in a rural community with low environmental and socioeconomic conditions is associated with low parental nutritional status, intrauterine and postnatal growth retardation and late weaning. Physical capability in adulthood is an indicator of pathological ageing trajectories. Our results stress the importance of promoting health conditions during development as a means to prevent future pathological ageing trajectories.

Abbreviations

PC: Physical capability; LB: Live births; SES: Socioeconomic status; HGS: Hand grip strength; GS: Gait speed; ChS: Chair stand test; SB: Standing balance; BMI: Body mass index.

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In memoriam

Joaquín Cravioto, José Luis Arredondo.

Authors' contributions

PA, conception, design, coordination, acquisition of data, and drafted the manuscript. MEA, design, statistical analysis, interpretation of data, and drafting the manuscript. VMM, acquisition and interpretation of data. JCGV, design, and molecular genetic studies. LPR, design of the informatic platform and data acquisition. CCT, curation and acquisition of data. CSP, clinical laboratory analysis. LMGR, design, and final approval of the manuscript. All Authors have read and approved the manuscript.

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Availability of data and materials

The data sets generated and/or analyzed during the current study are not publicly available due to patient privacy, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All participants provided written informed consent about the study, the genetic data and personal information security. Enrollment and consent procedures for this study were approved by the institutional review boards of Bioethics and Research of INGER, and Bioethics and Research Board of the National Institute of Pediatrics (INP), under the number of INP-INGER 06/2018. All methods employed in the study were performed in accordance with the relevant international guidelines and regulations, as well as those from the Ley General de Salud of Mexico.

Consent for publication

Not relevant.

Competing interests

The authors declare that they have no competing interests.

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