Iran J Public Health, Vol. 51, No.4, Apr 2022, pp.961-963

Letter to the Editor

Paternal Age at Birth and Hemoglobin Levels in Early Adolescents: A Nationwide Survey

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(Received 11 Nov 2020; accepted 24 Nov 2020)

Dear Editor-in-Chief

Adolescents are highly vulnerable to anemia because of increased nutritional demands accompanying the adolescent growth spurt and onset of menstruation in females. Anemia in this age group has been associated with diverse adverse health outcomes, such as impaired cognitive development, physical capacity, and immunity, which may persist throughout life (1). Several factors predisposing to anemia in adolescence have been suggested, including low socioeconomic status, perinatal complications, and poor postnatal nutrition (2). Recently, the prenatal environment—specifically, advanced parental age—has been implicated in the development of hematologic disorders. Combined results from 16 studies included in the Childhood Leukemia International Consortium have suggested a linear increase in the risk of childhood leukemia with advanced paternal age (3).

Most previous studies regarding anemia have focused on environmental or nutritional factors in developing countries. These studies reported that children of younger mothers are vulnerable to anemia because of unfavorable socioeconomic conditions (4, 5). We thereby conducted a study to examine the effects of parental age on the prevalence of anemia in adolescents in a developed country.

Data were collected from the 2007–2016 Korean National Health and Nutrition Survey, which is a nationwide representative cross-sectional survey with a stratified, multistage, probability sampling design. We identified 4,170 adolescents (aged 10–18 years) who were at least 12 years younger than their parents and for whom data were available regarding the age of both parents. Our outcome of interest was the serum hemoglobin (Hb) level. Data were obtained from the Health Interview and the Health Examination regarding the participant's Hb, age, sex, and body mass index (BMI); the household's income quartile; and the parents' smoking history, BMI, and ages.

The median age of participants was 13 years (interquartile range, 11–14), and 53.4% were male. Mean Hb levels were 14.4 ± 1.1 for males and 13.4 ± 0.9 for females. Median parental age at birth was 29 years for mothers and 32 years for fathers. Maternal age and paternal age were closely associated with each other. To identify factors associated with Hb levels, stepwise multivariate regression models were applied, accounting for the participants' age, sex, BMI, and economic status, as well as parental characteristics. The beta coefficients were 0.13 for participant's age (per 1-year increase, $P < 0.001$), 0.99 for male sex of the participant (*P*

< 0.001), and 0.01 for paternal age (per 1-year decrease, $P = 0.018$). Participant BMI and economic status and parental smoking history, BMI, and maternal age were not significantly associated with the serum Hb. Multivariate regression analysis revealed that advanced paternal age at birth was associated with low Hb during adolescence (Fig. 1, for trend, $P = 0.026$).

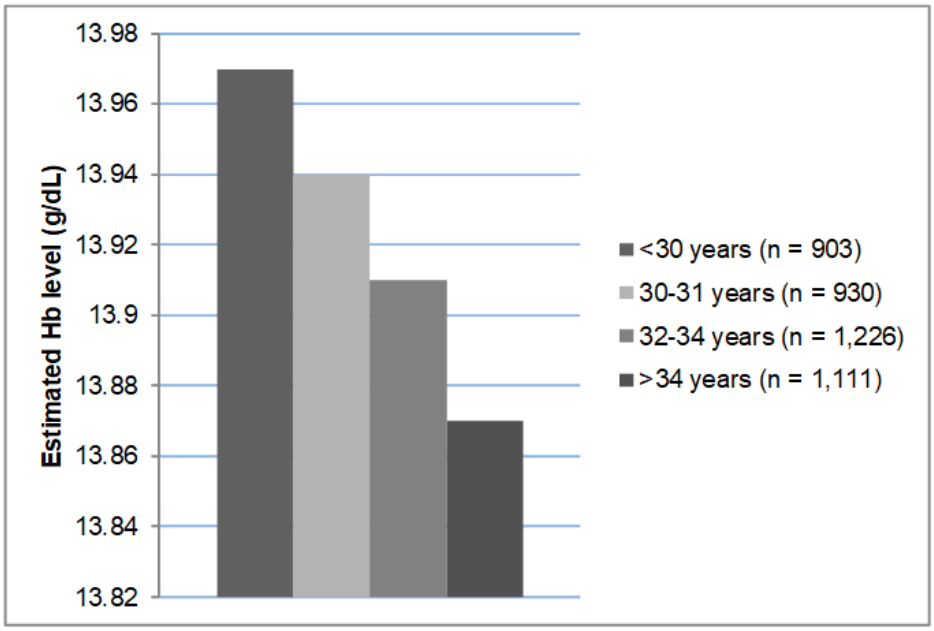

Fig. 1: Hemoglobin (Hb) levels in adolescents according to paternal age.
$P = 0.026$ for trend in multivariate regression analysis, adjusting for adolescents' age (continuous) and sex

The recent increase in parental age at first delivery has raised concerns because of potential adverse consequences affecting the health of the offspring. Although less well studied than maternal age, advanced paternal age has been associated with a wide range of health and developmental effects (6). Genomic sequencing studies have shown higher numbers of de novo mutations and decreased DNA methylation patterns in individuals with older fathers at birth (7), potentially increasing their vulnerability to hematologic disease. Furthermore, paternal, but not maternal, age at birth has been positively linked to leukocyte telomere length of the children (8). Results from a prospective study suggested that longer telomere length was associated with an increased risk of non-Hodgkin lymphoma (9). Thus, the association between adolescent anemia and older paternal age may reflect aberrant hematopoiesis in individuals with older fathers (10).

This snapshot study adds to the growing body of evidence of possible hematologic abnormalities in the children of older fathers. Further data from longitudinal studies regarding advanced paternal age and hematologic abnormalities are required to confirm and explain our results.

Acknowledgements

This work was supported by the Gachon University Gil Medical Center (Grant no. FRD2021-14). The funder had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript. Jae Hee Choi and Ki Dong Ko contributed equally to this work as a first author.

Conflict of interest

The authors declare that there is no conflict of interests.

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