



## POTENTIAL FACTORS FOR THE DEVELOPMENT OF KIDNEY DISEASE IN ADOLESCENTS AND YOUNG PEOPLE: INTEGRATIVE REVIEW

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### ABSTRACT

**Objective:** to identify scientific evidence on the potential factors for the development of chronic kidney disease in adolescents and young people. **Method:** integrative review, using a selection form for extraction of research data in the databases: Latin American and Caribbean Literature on Health Sciences, National Library of Medicine and Web of Science, accessed via the Coordination for the Improvement of Higher Education Personnel portal, in the period of August 2021, which included 12 articles. The analysis of the review results occurred from the synthesis of each primary study. **Results:** scientific evidence pointed out, as potential factors for the development of chronic kidney disease in adolescents and young people, the chronic diseases, such as diabetes, hypertension and obesity, as well as the risk factors, such as painkiller use, overweight, low birth weight and prematurity. **Conclusion:** it was concluded that it is necessary to follow-up, from collective or individual health education strategies, these adolescents, young people and their families, because chronic diseases and risk factors can be prevented or controlled.

**Keywords:** Adolescent. Chronic disease. Kidney diseases.

### INTRODUCTION

Adolescence is an important period of human growth and development, with bodily and emotional changes, through a process of biopsychosocial maturation, with manifestations of new feelings, attitudes and discoveries, with the construction of one's own identity<sup>(1)</sup>. Youth already present a more consolidated social identity according to their cultural and relational context, where, most of the time, individuals have more responsibilities and expand their occupations<sup>(2)</sup>.

The World Health Organization (WHO) classifies the period between 10 and 19 years, 11 months and 29 days of age as adolescence, and understands the period between 15 and 24 years as youth<sup>(3)</sup>. Chronic disease in adolescents and young people determines changes in their daily lives, in addition to restrictions caused by the disease itself, which require constant care and adaptation to this new situation<sup>(4)</sup>. Among chronic diseases, there is Chronic Kidney Disease (CKD), which is among the diseases

that affect adolescents and young people. It is a disease of progressive evolution, with changes and limitations that can generate social and psychological conflicts<sup>(1)</sup>. In Brazil, according to the Brazilian Institute of Geography and Statistics (IBGE, as per its Portuguese acronym), in 2019, the Brazilian population was 210.14 million; of these, 54.488 million were CKD patients and, according to the 2019 Census of the Brazilian Society of Nephrology (SBN, as per its Portuguese acronym), 0.8% are between 13-19 years old and 20.8% are between 20-44 years old. This census had the participation of only 314 of the 805 renal units registered with the SBN, being that, in Brazil, in 2019, the total number of dialysis patients was estimated at 139,691<sup>(5)</sup>.

Chronic disease, such as CKD, and its treatment make significant changes in the lives of adolescents and young people. Adaptations, such as dietary restrictions and family reorganization, are necessary, causing not only imbalances in the body, but also impacts on social relationships and with peers<sup>(1,6)</sup>. The

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social, emotional and psychological changes experienced by these adolescents and young people may be more significant than the clinical changes, thus generating fear, fragility and the prospect of death<sup>(7)</sup>. In this sense, it is important to know the scientific evidence found in the literature in order to support an assistance for the prevention of diseases and promotion of quality of life of adolescents and young people who have potential factors for CKD. Accordingly, the objective of this review study is to identify scientific evidence on the potential factors for the development of chronic kidney disease in adolescents and young people.

## METHOD

This is an integrative review study<sup>(8)</sup>, which sought answers to this research question: which chronic diseases and potential risk factors can lead adolescents and young people to develop chronic kidney disease? This question was developed from the elements of the PICOT strategy (population/patient – P: adolescents and young people with chronic diseases; intervention

– I: chronic diseases and risk factors; comparison – C: not applicable; and results (outcome) – O: chronic kidney disease; time or chronology – T: not applicable). Sampling took place in the Latin American and Caribbean Literature on Health Sciences (LILACS) database, through the Virtual Health Library (VHL) Regional Portal, National Library of Medicine (PubMed) and Web of Science, accessed via the Coordination for the Improvement of Higher Education Personnel (CAPES, as per its Portuguese acronym) portal.

Inclusion criteria included research articles on the theme that answered the review question, in English, Spanish or Portuguese, with no time limits. The search in the databases took place in August 2021. Numerous search strategies were used to find the two that best addressed the review question, as shown below (Table 1). There were 485 records in the LILACS database, 822 in PubMed, and 289 in Web of Science, totaling 1,596 records. Initially, the titles and abstracts that met the inclusion criteria were read, totaling 12 articles.

**Table 1.** Database and search strategy, Santa Maria, Brazil, 2021

| Database   | Search strategy   |
|--|---|
| Latin American and Caribbean Literature on Health Sciences (LILACS) and PubMed | adolescent OR youth AND “disease, chronic” AND “kidney disease” |
| Web of Science   | adolescent AND “kidney disease” AND “risk factors”              |

**Source:** Table designed by the author.

In order to perform the data extraction of the research studies, two instruments were used. The first, made by two reviewers, double independent, is a table with the article indicator number, reference and inclusion criteria: not an article (NA), not in the language (NL), not research (NR), not from the theme (NT) and not answering the question (NQ) (review question). The second is a table with the information of the article indicator number, reference, research objective, design, results and level of evidence<sup>(9)</sup>.

As for the level of evidence of the study, the hierarchical classification considered the type of research question of the selected articles. When the question is related to treatment/intervention, there is a hierarchical classification in seven levels; when it is related to prognosis/etiology, in five levels; and when it refers to meaning/experience/understanding of the user,

in five levels. The interpretation of the results was based on the answer to the review question. The presentation of the review comprises the synthesis of knowledge, developed by the relationship of chronic diseases and risk factors that can cause CKD in adolescents and young people. These steps constitute the results and the discussion. Regarding the ethical aspects, the Legislation on copyright laws (Nº 9,160, dated February 19, 1998) was respected.

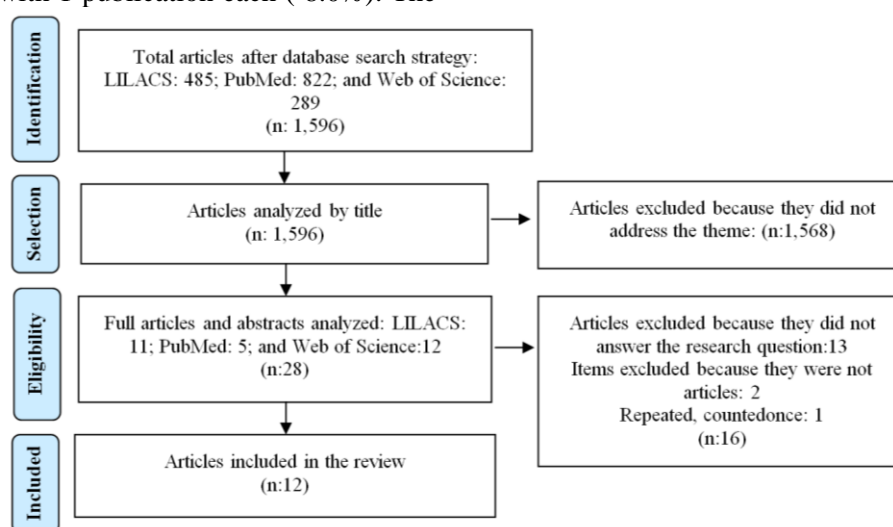
## RESULTS

When characterizing the studies, it was found that the publications of articles occurred as follows: in 2010, with 1 article (8.0%); 2012, with 2 articles (16.0%); 2015, 2016, and 2017, with 1 article in each year (8.0%); 2018 and 2019, with 2 articles in each year (16.0%); 2020,

with 1 article (8.0%); and 2021, with 1 article (8.0%). Thus, in the period 2015-2021, there were 9 (75.0%) articles published, which demonstrates the growth of interest in studies on the theme in recent years. The articles covered by this research were developed as of 2010. Regarding the country of the studies, the United States (USA) stood out with more publications: 4 (33%), followed by Japan, with 2 publications (16.0%), and Chile, China, Canada, Israel, Iran and Brazil, with 1 publication each (8.0%). The

articles found were from the health area – one from medicine/psychology and all the others from medicine.

In the search, a total of 1,596 productions were located, of which 12 were included in the corpus of the study. As for exclusions, part of the productions were related to other diseases in adolescence. The flowchart (FIG. 1) describes the selection of articles for the integrative review, based on the PRISMA model<sup>(10)</sup>.



**Figure 1.** Flowchart of the article search and selection process.

**Source:** Figure designed by the author based on the PRISMA diagram (MOHER et al., 2015).

In Table 2, the characteristics of the articles regarding title, authors, country, year of publication, objective, design (study approach,

participants) and level of evidence (LE) are displayed.

**Table 2.** Characteristics of the articles selected for integrative review.

| AUTHOR/<br>YEAT                         | COUNTRY | OBJECTIVE   | DESIGN  | LE/<br>NQ |
|---|---------|---|---|-----------|
| Sanderson<br>KR. 2020 <sup>(11)</sup>   | USA     | To characterize the prevalence and predictors of microalbuminuria, high blood pressure and/or abnormal kidney volume in adolescence.  | QT<br>42 participants, adolescents, who were born before the 28 <sup>th</sup> week of pregnancy.                        | L2/P      |
| Murai-Takeda<br>A. 2019 <sup>(12)</sup> | Japan   | To investigate the specific effect of gender and low birth weight on kidney function.   | QT<br>2,417 Japanese adolescents (males 1,736; females 681), aged 15-16 years, were assessed over 8 years (2007-2014).  | L2/P      |
| South AM.<br>2019 <sup>(13)</sup>       | USA     | To compare blood pressure (BP) and kidney function in adolescents aged 14 years old, who were preterm infants with very low birth weight (VLBW, <1,500 g), with their full-term peers and assess whether obesity and gender modify these relationships.                                   | QT<br>Adolescents 14 years old born preterm with very low birth weight (n = 96) compared to full-term peers (n = 43).   | L2/P      |
| Kanda T.<br>2018 <sup>(14)</sup>        | Japan   | To investigate changes in birth weight and Glomerular Filtration Rate (GFR) between 1998 and 2015 in healthy Japanese adolescents (15-16 years old). To examine trends in the birth weight category to determine the contribution of birth weight changes on rates of kidney dysfunction. | QT<br>3,737 Japanese male adolescents (15-16 years old) using annual sectional data over an 18-year period (1998-2015). | L2/P      |

To be continued...

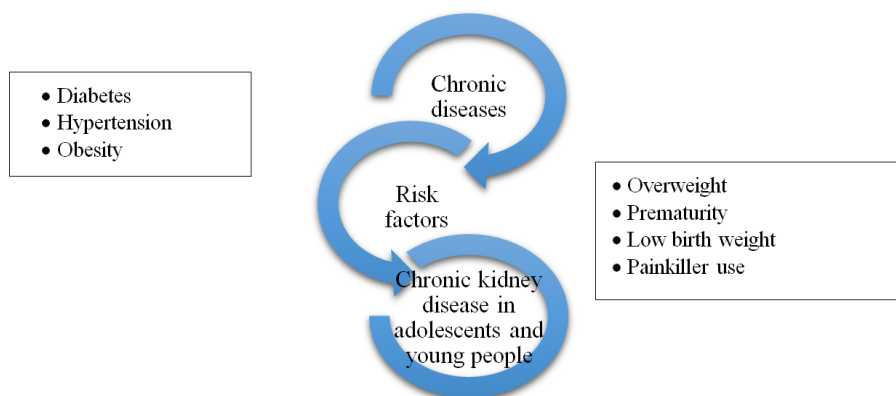
|                                    |        |   |   |      |
|------------------------------------|--------|---|---|------|
| Tajbakhsh R. 2017 <sup>(15)</sup>  | Iran   | To assess the association of Glomerular Filtration Rate (GFR) with cardiometabolic risk factors in Iranian adolescents.   | QT<br>367 adolescents between the ages of 10 and 18.  | L2/P |
| Khalsa DDK. 2016 <sup>(16)</sup>   | USA    | To analyze, during the adolescent phase, whether low birth weight infants have an increased risk of Chronic Kidney Disease (CKD).   | QT<br>5,352 participants aged 12-15 years in the National Health and Nutrition Examination Survey, 1999-2012.   | L2/P |
| Vivante A. 2012 <sup>(17)</sup>    | Israel | To assess the association between BMI in adolescence and the risk of End-Stage Renal Disease (ESRD) from all causes, diabetic and non-diabetic.   | QT<br>1,194,704 17-year-old adolescents who were screened for military service between January 1, 1967 and December 31, 1997.   | L2/P |
| Dart AB. 2012 <sup>(18)</sup>      | Canada | To assess renal outcomes and survival in young people with type 2 diabetes (DM2) versus type 1 diabetes (DM1) versus non-diabetic control individuals.  | QT<br>342 prevalent young individuals (ages 1 to 18) with DM2, 1,011 young individuals with DM1 and 1,710 control individuals identified from 1986 to 2007.   | L2/P |
| Saboia, ZMRM. 2018 <sup>(19)</sup> | Brazil | To investigate the association between syndecan-1 and kidney function in overweight adolescents.  | QT-QL<br>56 adolescents aged 14 to 19 years (18 boys and 38 girls).   | L2/P |
| Sánchez G.JP. 2010 <sup>(20)</sup> | Chile  | To quantify the direct and indirect risk factors that affect the development of CKD   | QT<br>164 first- to third-year medical students from the Austral University of Chile under the age of 25.   | L2/P |
| Zeller MH. 2015 <sup>(21)</sup>    | USA    | To assess the links among comorbid health status, severe overweight and weight-related quality of life (WRQOL) in severely obese adolescents undergoing weight loss surgery (WLS) to inform clinical care.  | QT<br>242 adolescents (aged 13-19 years) (February 2007 to December 2011).  | L2/P |
| Wang Y. 2021 <sup>(22)</sup>       | China  | To identify the risk factors for the development and progression of kidney disease in a Chinese population group. It also aimed to examine whether the impact of risk factors on CKD has changed over time. | QT-QL<br>2,432 hypertensive adolescents who lived in Hanzhong. A subgroup of 202 individuals was further analyzed over a 12-year period from 2005 to 2017, in order to determine risk factors for the development and progression of CKD. | L2/P |

**Caption:** (QL) Qualitative; (QT) Quantitative; (LE) Level of Evidence; (CQ) Clinical Question; (P) Classification from clinical questions related to prognosis or etiology.

**Source:** Table designed by the author.

As for the level of evidence, there was a predominance of level 2 in the articles found, with the clinical question directed to prognosis, demonstrating the interest in understanding the probability of the occurrence of certain results, which enables knowledge about what determines the evolution of a certain disease.

The articles found were analyzed and grouped by similar data (FIG. 2), which allowed to highlight chronic diseases and some risk factors as potential factors that may lead adolescents and young people to develop CKD.



**Figure 2.** Evidence on risk factors and chronic diseases that can cause CKD in adolescents and young people. LILACS, PubMed and Web of Science, Santa Maria, RS, Brazil, 2021.

**Source:** Figure designed by the author.

## DISCUSSION

The main chronic diseases found were Diabetes Mellitus (DM), Systemic Arterial Hypertension (SAH) and obesity. The risk factors that appeared in the studies were painkiller use, overweight, Low Birth Weight (LBW) and prematurity. A study that assessed young people with diabetes – type 2 diabetes (DM2) versus type 1 diabetes (DM1) and a control group of non-diabetics – revealed that those with DM2 had a 4-fold increased risk of progressing to kidney failure compared to those with DM1, and a 23-fold increased risk of kidney failure and 39-fold increased risk of dialysis compared to control individuals. Accordingly, a high risk of young people with DM2 developing CKD is pointed out<sup>(18)</sup>.

Furthermore, a Chinese cross-sectional study of 2,432 adolescents with hypertension living in Hanzhong City analyzed a subgroup of 202 individuals over a 12-year period from 2005 to 2017 and revealed that Systemic Arterial Hypertension (SAH), Diabetes Mellitus (DM) and Body Mass Index (BMI) were listed as important risk factors for the development and progression of CKD in these adolescents<sup>(22)</sup>.

Another study with 164 young people showed that 28% (n:50) self-medicated at least once a week with some type of painkiller, 32% (n:52) had BMI > 25, 48% (n:78) had family history of overweight or obesity, 52% (n:86) of SAH and 27% (n:44) of DM2. SAH, DM and painkiller consumption were considered as direct risk factors for the development of kidney disease<sup>(20)</sup>. Furthermore, studies show that overweight and obese adolescents are more likely to have reduced kidney function<sup>(15,17,19,20)</sup>. The relationship between BMI and risk for the development of end-stage CKD was assessed in 1.2 million 17-year-old adolescents over 30 years; and, at that time, the overall incidence rate of CKD was 2.87 cases per 100,000 person-years. In turn, in adolescents with normal weight, when compared to adolescents with obesity and overweight, a high future risk for end-stage CKD was identified, with incidence rates of 6.08 and 13.40 cases per 100,000 person-years, respectively<sup>(17)</sup>.

In an assessment among 56 adolescents (ranging in age from 14 to 19 years), a high

proportion of overweight adolescents (19.3%) and a considerable link between kidney function and endothelial damage, marked by syndecan-1 levels, were revealed. Possible kidney injury is indicated, since increased syndecan-1 had a significant relationship with markers of kidney function, such as Glomerular Filtration Rate (GFR), creatinine and urea<sup>(18)</sup>. Another “Teen-LABS” study, with 242 adolescents with severe obesity, analyzed before bariatric surgery, showed the presence of microalbuminuria in 14% of the surveyed participants, macroalbuminuria in 3%, estimated GFR (eGFR) < 60 mL/min/1.73m<sup>2</sup> in 3% and GFR > 150 mL/min/1.73m<sup>2</sup> in 7.1%. It was found that BMI values and the Homeostasis Model Assessment for insulin resistance (HOMA-IR) value were significantly associated with lower eGFR, being that, 3 years after the surgery, there was a significant improvement in the average eGFR<sup>(21)</sup>.

Japanese studies found that LBW is a worldwide public health problem, which demonstrated an increasing incidence in developed countries, being considered as a risk factor for CKD in adolescents and young citizens. Furthermore, both genders of adolescents and young individuals showed significant decrease in estimated GFR rates related to reduced birth weight<sup>(12,14,16)</sup>. To that end, high Blood Pressure (BP), decreased GFR and the prevalence of increased proteinuria occurred more frequently in adolescents with low birth weight and very low birth weight<sup>(14,16)</sup>.

Another risk factor is prematurity, being associated with decreased number of nephrons and increased risk of CKD. In the study with participants who were born before the 28<sup>th</sup> week of pregnancy and were assessed when they turned 15 years old, 50% of the sample had at least one renal abnormality (microalbuminuria, high blood pressure and/or kidney hypoplasia)<sup>(11)</sup>. In another study, prematurity was associated with high blood pressure and reduced kidney function, which were detected in adolescence. When compared to full-term newborns, preterm infants had higher Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP), lower GFR and higher urinary creatinine<sup>(13)</sup>.

The prevalence of SAH and DM have a significant prominence in CKD. In addition,

DM2 and SAH have been signaled as the main causes of kidney failure in patients undergoing treatment for CKD<sup>(23,24)</sup>. It is also noted that SAH and DM are indicated as the main primary causes of CKD<sup>(22,25)</sup>. It is also known that painkillers are within the group of Nonsteroidal Anti-inflammatory Drugs (NSAIDs), belonging to a class of drugs most used worldwide, used as analgesics, antipyretics and anti-inflammatories; and that, when used inappropriately, such as daily use for more than 1 year, they directly affect kidney function by decreasing prostaglandins, thus increasing the risk for the development of CKD. Furthermore, it was found that renal impairment is one of the main factors responsible for the high rate of morbidity and mortality associated with their indiscriminate use<sup>(26,27)</sup>.

Obesity is pointed out as a chronic disease caused by multiple factors, with risk of progressing to other chronic diseases. With it, there is an increase in the prevalence of SAH, DM, cardiovascular diseases and dyslipidemias<sup>(28,29)</sup>. In addition, people who were overweight at an early stage in life or who acquired obesity in adolescence have a higher risk of developing CKD in adulthood<sup>(30)</sup>. The WHO defines, as normal weight, the BMI between 18.5 and 25 kg/m<sup>2</sup>; a BMI between 25 and 30 kg/m<sup>2</sup> is considered as overweight; and a BMI > 30 kg/m<sup>2</sup> as obesity. It should be underlined that a high BMI is one of the most intense risk reasons for the development of a new case of CKD<sup>(31)</sup>.

LBW and prematurity are also risk factors for CKD<sup>(32)</sup>. People born at term but with LBW may be at high risk for hypertension, albuminuria and CKD in the future<sup>(33)</sup>. LBW, as established by the WHO with a weight of less than 2,500g, is related to infant mortality, and is therefore considered as a public health problem<sup>(34)</sup>. Furthermore, preterm birth can cause several complications, including acute kidney injury, which is compounded by the anatomical and physiological immaturity of the premature child's kidney<sup>(35)</sup>. It should be highlighted that premature babies are more likely to develop kidney disease years later, a statement justified by both observational cohort studies and case reports. Furthermore, children who have suffered

Acute Kidney Failure (AKI) due to various conditions may, in the long term, develop CKD.

Accordingly, it is increasingly apparent that kidney disease in adulthood often begins in childhood<sup>(33)</sup>, and the results of this review may contribute to the knowledge of chronic diseases and risk factors as potential factors for adolescents and young people to develop CKD.

There were few studies on this theme with this population – in the case of this research, only one Brazilian study was found. It is noteworthy that these studies provide data for the follow-up of youth and adolescents with these potential characteristics, corroborating the prevention of the development of CKD in adolescents and young citizens.

## CONCLUSION

It was concluded that scientific evidence pointed to chronic diseases, such as DM, SAH and obesity, as well as risk factors, such as painkiller use, overweight, LBW and prematurity, as potential factors for the development of CKD in adolescents and young people. Overweight and obesity, considered as worldwide epidemics, when associated with DM and SAH, are responsible for intensifying the risk for CKD. In addition, painkillers, belonging to the class of NSAIDs, when used abusively, may cause mild and transient dysfunction and even chronic kidney disease, since they inhibit prostaglandin synthesis, thus undermining the renal blood flow and favoring ischemic injury. Accordingly, the risk-benefit of its use must be assessed, considering the probable adverse effects. Furthermore, low birth weight and prematurity also stood out as possible predisposing factors for adolescents and young people to develop CKD, requiring continuous follow-up, in order to identify early signs of kidney disease, aiming at prevention and efficient treatment. In light of this context, for prevention purposes, it is necessary to follow-up adolescents and young people affected by these chronic diseases and who present these risk factors for the development of CKD. It is considered that both adolescents and youth can adopt a lifestyle that will reflect positively in their adulthood, preventing themselves from developing diseases.

## FATORES POTENCIAIS PARA DESENVOLVIMENTO DE DOENÇA RENAL EM ADOLESCENTES E JOVENS: REVISÃO INTEGRATIVA

### RESUMO

**Objetivo:** identificar evidências científicas acerca dos fatores potenciais para o desenvolvimento de doença renal crônica em adolescentes e jovens. **Método:** revisão integrativa, utilizando uma ficha de seleção para extração dos dados das pesquisas nas bases de dados: Literatura Latino Americana e do Caribe em Ciências da Saúde, National Library of Medicine e Web Of Science, acessada via portal Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, no período de agosto de 2021, o que incluiu 12 artigos. A análise dos resultados da revisão ocorreu a partir da síntese de cada estudo primário. **Resultados:** as evidências científicas apontaram, como fatores potenciais para o desenvolvimento de doença renal crônica em adolescentes e jovens, as doenças crônicas, como diabetes, hipertensão, obesidade, e os fatores de risco, como uso de analgésicos, sobrepeso, baixo peso ao nascer e prematuridade. **Conclusão:** concluiu-se que é necessário um acompanhamento, a partir de estratégias coletivas ou individuais de educação em saúde, desses adolescentes, jovens e suas famílias, pois as doenças crônicas e fatores de risco podem ser prevenidos ou controlados.

**Palavras-chave:** Adolescente. Doença crônica. Nefropatias.

## POSIBLES FACTORES PARA EL DESARROLLO DE LA ENFERMEDAD RENAL EN ADOLESCENTES Y JÓVENES: REVISIÓN INTEGRADORA

### RESUMEN

**Objetivo:** identificar evidencias científicas acerca de los posibles factores para el desarrollo de enfermedad renal crónica en adolescentes y jóvenes. **Método:** revisión integradora, utilizando una ficha de selección para recolección de los datos de las investigaciones en las bases de datos: Literatura Latinoamericana y del Caribe en Ciencias de la Salud, National Library of Medicine y Web Of Science, accedida a través del portal Coordinación de Perfeccionamiento de Personal de Nivel Superior, en el período de agosto de 2021, lo que incluyó 12 artículos. El análisis de los resultados de la revisión ocurrió a partir de la síntesis de cada estudio primario. **Resultados:** las evidencias científicas señalaron, como factores potenciales para el desarrollo de enfermedad renal crónica en adolescentes y jóvenes, las enfermedades crónicas, como diabetes, hipertensión, obesidad, y los factores de riesgo, como uso de analgésicos, sobrepeso, bajo peso al nacer y prematuridad. **Conclusión:** es necesario un acompañamiento, a partir de estrategias colectivas o individuales de educación en salud, de esos adolescentes, jóvenes y sus familias, pues las enfermedades crónicas y los factores de riesgo pueden ser prevenidos o controlados.

**Palabras clave:** Adolescente. Enfermedad crónica. Nefropatías.

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