Early age at menarche and chronic kidney disease; an updated mini-review

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Abstract
Chronic kidney disease (CKD) is one of the most important causes of pediatric morbidity, related to more mortality, and could result in severe psychosocial damages, a negative self-image and a feeling of inferiority compared to their normal peers (1). The prognosis of CKD in adolescents is poor, because disease progression to a higher CKD stage may be occurred in a considerable number of children, especially in the patients with advanced CKD (2). In addition, CKD could increase the risk of cardiovascular morbidity and mortality (3). CKD has many risk factors such as genetics (4), positive family history (5), gender [a controversy; more in men (6) or women (7)], ethnicity (more in blacks and African-Americans) (8), age (decreasing by age in both men and women) (9), low-birth weight (10), obesity (11), low socioeconomic status (12), smoking (13), diabetes (14), hypertension (14), acute kidney injury (AKI) (15), nephrotoxins (16), obstructive sleep apnea (17), heart rate (18), periodontal diseases (gram-negative-tooth-associated microbes) (19) and uric acid levels (20). Thus, the identifying of the CKD risk factors and screening of at-risk populations will rise early detection. Moreover, starting the early treatment of modifiable risk factors of CKD will affect the cost of renal replacement therapy.

Materials and Methods
For this mini-review, we used a variety of sources including Web of Science, PubMed, Embase, Scopus and directory of open access journals (DOAJ). The search was performed by using combinations of the following key words and or their equivalents; “chronic kidney disease”, “age at menarche”, “growth retardation”, “diabetes mellitus”, “hypertension”, “acute kidney injury”, “nephrotoxins”, “childhood”, “nutritional status”, and “malnutrition”.

Introduction
Chronic kidney disease (CKD) is one of the most important causes of pediatric morbidity, related to more mortality, and could result in severe psychosocial damages, a negative self-image and a feeling of inferiority compared to their normal peers (1). Earlier age at menarche (AAM) is related to higher risk of diabetes and then higher CKD risk. Many factors may contribute to the relationship between puberty and CKD such as malnutrition and growth hormone. There also is a growth retardation among children with CKD which is associated with higher morbidity and mortality.

Keywords: Chronic kidney disease, Age at menarche, Growth retardation, Diabetes mellitus, Hypertension, Acute kidney injury, Nephrotoxins, Childhood, Nutritional status, Malnutrition

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Earlier age at menarche
Earlier age at menarche (AAM) may be related to higher risk of diabetes (21) and then higher CKD risk (14). Approximately half of children with CKD have delayed puberty and late AAM (22). Like many other chronic diseases, CKD may delay puberty and further late AAM (23) including later height and reproductive capacity (24). The biological changes of puberty can in turn directly affect on the kidney (25). In addition, although it was primarily suggested that the years before puberty may be protected from the effects of hyperglycemia (26), acceleration of kidney dysfunction during puberty has been reported in diabetes mellitus (27). Many factors may contribute to the relationship between puberty and CKD such as malnutrition (23) and growth hormone (GH) (28). In addition, the children receiving GH therapy had similar rate of CKD compared to children without CKD, despite primary fear about adverse effects of GH on kidney function (29). Moreover, considering the importance of hypothalamus in the control of initiation and continuation of puberty growth, it is supposed that CKD could affect these processes (30). Furthermore, untreated CKD may result in lesser derangements in kidney function, coma and even effect on brain (30).
Generally, almost half of children with dialysis are under the third percentile of height and this decline will continue during dialysis (30). Additionally, children with CKD often have two years lag in the initiation of sexual maturation compared to their peers (28).

There is also a growth retardation among children with CKD which is associated with higher morbidity and mortality (31). These children have higher rates of infections, shorter stature and hospitalizations too (32). In addition, it has been suggested that the observed growth retardations were influenced by metabolic and nutritional factors (33,34). Similarly, the age of initiation of CKD and renal function are mainly related to the level of growth retardation (35). Growth failure is a substantial problem among adolescents with CKD which is originated from many factors encountered because of the primary disease or secondary to the renal impairment (36). CKD can cause impairment at any level of development from fetus to adolescence and further growth retardation (37). With a prolonged duration of CKD, the degree of height deficit would be even worsened (37). In fact, malnutrition and growth retardation are main significant problems in CKD adolescents which are associated with the degree of kidney failure and treatment options (38). There is also a short stature in CKD patients treated with GH hormone (39).

There are different mechanisms for explaining the factors affecting the growth in childhood CKD including endocrine disturbances and nutritional problems (36). These patients may have some abnormalities of their body composition which might not be detectable by a simple measurement of body mass index (BMI) (36). Moreover, the peritoneal dialysis will result in a better growth than hemodialysis in CKD children (38).

For many of children with CKD, the supplementary feeding is essential in order to maintain sufficient electrolyte, water and nutrient requirements (33). Therefore, these patients in the predialysis stage, in order to prevent metabolic disorders among them, may be supported by early nutritional intervention, which in turn might be resulted in appropriate growth rates (34). In fact, adolescents with CKD may have some mental disorders and low quality of life compared to normal people (1,40).

These patients have reported higher levels of depression, stress and feeling of hopelessness correlated with their conditions and limitations (41).

Despite improvements in the management of adolescents with CKD, there are various neurocognitive deficits among these patients, even after correction of nutrition, metabolic acidosis and renal osteodystrophy and further improvement in growth (42). In addition, having excess weight in early life or being overweighted between puberty and age 20 years are related to CKD in the following years. Thus, declining the weight in the early life can reduce the probability of CKD later in life (43,44). Accordingly, the management of nutrition and its relationship with growth process is complex.

**Conclusion**

Therefore, it is necessary to assess accurately body composition in CKD patients to understand the potential problems. Furthermore, in infants with CKD, untreated disease is accompanied by a severe growth retardation with a monthly loss in height during the first year of life.

**Author's contribution**

MA is the single author of the paper.

**Conflicts of interest**

The author declares no conflict of interest.

**Ethical considerations**

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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