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Review

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Factors that Influence Taste Disorders Affect Salt Intake in Chronic Kidney Disease

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ABSTRACT

High sodium intake influences the development of chronic kidney disease (CKD). Various factors can influence sodium consumption, one of which is impaired taste perception. This study aims to evaluate factors influencing taste disorders and the impact of high intake of sodium, saliva, and zinc, especially in CKD patients. The method used involved searching for articles using Google Scholar, PubMed, EBSCO, and ProQuest search engines. The inclusion, exclusion criteria, and journal selection method, using Problem/Population, Intervention, Comparison, Outcome form and Prisma Flow Diagram, focused on experimental studies in the last ten years (2013-2023) with specific search keywords. A total of 28 suitable articles matched the criteria. The results revealed three sub-themes: (A) Factors affecting sodium intake: Taste disorder/dysgeusia in CKD, (B) Effect of zinc on sodium intake or CKD, and (C) Effect of sodium on CKD. This study discusses the three most significant factors that influence taste distortion: salt intake, saliva quality, and zinc deficiency, besides old age. Taste disorders due to old age can be overcome with education and behavior planning. The habit of high sodium intake and saliva quality can be improved by reducing sodium intake, while the management of zinc deficiency is addressed through supplementation. In summary, tasting disorders in CKD are strongly influenced by high intake of sodium, saliva, and zinc deficiency.

Keywords: Chronic kidney failure, sodium, saliva, taste disorders, zinc deficiency

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INTRODUCTION

A diet with balanced and complete nutrition is required for a human's well quality of life. It should be noted that not proportionally nutrient intake, either excessive or deficient, might lead to organ or even damage. Thus, mineral intake in sodium (Na) or salt is recommended to be regulated for consumption in moderation or limited amounts. Indonesian Ministry of Health recommends the maximum salt intake is only one teaspoon or 2 g of Na or 5 g of salt per day. In addition, The Institute of Medicine which publishes the Dietary References Intakes (DRI) recommends Na intake in young adults of 1.5 g (65 mmol)/day or as much as 3.8 g salt. Further recommendations on the maximum tolerable limit for Na intake are 2.3 g (100 mmol)/day or 5.8 g of salt. According to the World Health Organization, Geneva, Switzerland 2012, the restriction of Na intake to less than 2.3 g/day corresponding to 5.8 g of salt (or 100 mmol) is one of the most cost-effective measures to improve public health. The average Na consumption of the Indonesian population is 3.5 g/day. The highest consumption is in the adult age group over 19 years, which is 3.7 g/day, and this has exceeded the recommended limit.[1] Excessive salt consumption could induce various disorders and diseases, such as increased blood pressure and hypertension. The close relationship between dietary Na and hypertension in the general population has been analyzed and reported by many studies.[2-4]

Salt consumption protocol should be a concern in the normal people population moreover in the group who has some specific precautions like kidney diseases. The salt reabsorption process mainly takes place in the kidney,[5] thus understanding the physiological role of kidney regulation in controlling salt levels is very important.

It is a general opinion that high salt intake causes an increase in blood pressure, and subsequently can cause impaired kidney function. However, it needs to be examined whether high salt consumption can directly worsen kidney function. The amount of salt consumed depends on the ability to detect and determine salty taste; it is necessary to examine what factors can affect taste perception, both in healthy subjects and CKD subjects.

This paper's purpose is to review the factors that affect taste disorders and the result of high salt intake, saliva, and zinc deficiencies in the subjects of CKD.

MATERIAL AND METHODS

A search for relevant full-text articles published from 2013 to 2023 was effectuated in online literature databases from Google Scholar, Medline database via the PubMed search engine, CINAHL database via EBSCO, and EMBASE database via ProQuest. The study question was created using the Problem/Population, Intervention, Comparison, Outcome (PICO) form (Table 1), as advised by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. The reason for determining the publication of the previous 10 years is to ensure the data obtained from the latest research results. A critical appraisal methodology was employed in the field of medical and health sciences to evaluate the presence of bias in the selected papers.

MAIN POINTS

- Taste perception can be impaired in several conditions, such as old age, high salt intake habits, poor saliva quality, and zinc deficiency. Taste perception disorders can occur in both subjects with chronic kidney disease(CKD) and normal subjects, but are significantly more common in CKD subjects, not depending on the stage of CKD and age, but are related to the duration of suffering from CKD.
- Habits of high salt intake can cause impaired taste perception, and this applies vice versa. High salt intake can not only cause hypertension which in turn causes CKD, but it can also directly cause kidney damage and increase the stage of CKD. The solution is limiting salt intake which can improve taste perception disorders, hypertension, and CKD stages.
- Impaired saliva quality can be improved by limiting salt intake, whereas zinc deficiency, which can cause impaired taste perception and hypoalbuminemia, which in turn affects the stage of CKD, needs to be met, either with supplementation or a diet high in zinc.
- For conditions that cannot be changed, such as age and gender, they are treated by providing education on good eating patterns and living habits.

RESULTS

The results of the literature search obtained 178 articles, then the selection was made to obtain the appropriate 28 articles (Figure 1).

The results based on the Prisma Flow Diagram procedure go through 3 stages, namely Identification, Screening, and Selected Articles. The results of selected articles amounted to 28 articles.

Results showed in 3 sub-themes (Table 1) Factors Influenced Taste Disorders/dysgeusia in CKD; (14 articles), (Table 2) Effects Zinc in Sodium intake or CKD (six articles) and (Table 3) Effects Sodium to CKD (eight articles).

Factors that Influenced Sodium Intake

Taste Disorders: According to Shim's research, impaired salt taste perception can occur in 42.1% of healthy subjects and 15% in smell disorders. According to research by Chewcharat, McMahon, Giugno, Konstantinova, Kim, and Vengalasetti, in normal subjects, there may be 17% taste dysfunction, but in non-dialysis CKD there is significant taste perception impairment, 30% olfactory impairment, and 13% taste dysfunction. Smell and taste disorders in CKD subjects were found to be related to muscle strength, on examination of grip strength. Tanaka et al's research states that taste disturbances in CKD patients undergoing dialysis are much more pronounced (>50%). Yusuf et al.,(2022) state that in Nigeria the ratio of hypogeusia in CKD and non-CKD is 27% versus 1%.

However, in Kim et al.'s study,[6] salt intake and salty taste preference in CKD stage 4 and 5 subjects were found better than in normal subjects, possibly because older patients were easier to educate, and CKD subjects with higher stage were more aware of the disease. Indeed, according to Melilo et al.,(2021)[7] taste perception disorders are not related to stage and age, but a significant predictor of taste dysfunction is the duration of suffering from CKD [OR 4.889]. Research shows that age and good education are important in salty taste preferences. Ahn and Wright's study on TPB proved that education for 36 months was effective in salt restriction. In the advanced program, the factors that could hinder the diet program were evaluated and identified, such as taste selection, social gathering, desire to be healthy, and an understanding of disease, so that the TPB of limiting salt intake was successful.

According to Shim and Fitzgerald's[8] study, impaired taste perception is associated with high natrium intake. Result of Manley's study, this disorder was also associated with saliva quality in CKD subjects. According to Mc Mahon's (2014)[9] study,

Table 1. Components Criteria for Inclusion Criteria for Exclusion Population CKD Patients

	Components Criteria for Inclusion	Criteria for Exclusion
Population	Chronic Kidney Disorder (CKD) patients, dialysis and Non-Dialysis	Patients having diseases other than CKD
Intervention	Studies on the effects of sodium, zinc, and taste disorders in CKD using Medical Subject Headings (MeSH): taste disorders, taste perception, taste threshold, salt preference, salty appetite, dysgeusia, sodium intake, zinc, from journals in English or other international languages, in peer-reviewed journals. All sorts of study designs, including mixed methods, quantitative, and qualitative, had been subject to peer review. Eligible original articles: good quality of experimental study.	Anything includes works without peer review, including reviews, blogs, book chapters, and website material. Review articles. Meta-analysis study Not eligible original articles
Comparator/control	CKD patients with observation/intervention/placebo	Without observation/intervention/placebo
Outcome	Quantitative and qualitative results about dysgeusia, taste disorders	No outcome

MeSH; Medical Subject Headings

taste disorders occur with CKD, not depending on age and gender but with specific impairment in salty tastes. Whereas Konstantinova's study stated that taste disorders correlated with duration of treatment and metallic taste in the sense of taste, and according to Chewcharat's study,[10] CKD correlated with olfactory dysfunction but not gustatory dysfunction.

Effects of Zinc in CKD: According to Tavares 2013, low plasma zinc levels in non-dialysis CKD patients are associated with the impaired perception of bitter, sour, and salty tastes. Zinc deficiency in addition to causing impaired taste perception resulting in increased sodium intake can also be a direct cause of decreased kidney function and the development of CKD

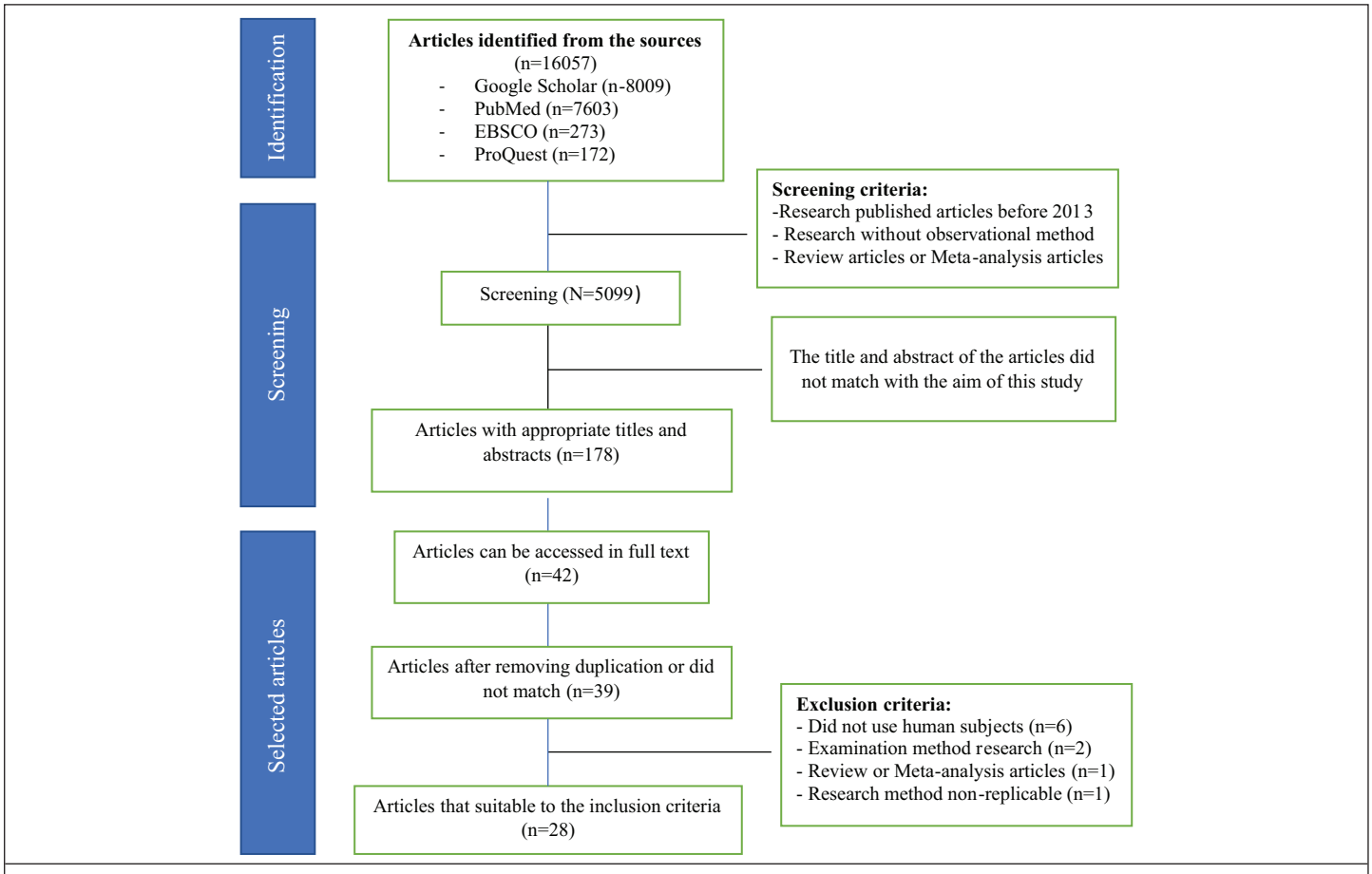

Figure 1. Prisma Diagram results of Review Factors Influence Taste Disorders in CKD.

Table 2. Factors Influenced Taste Disorders/Dysgeusia in Chronic Kidney Disease

No	Author	Aim of the Study	Participants and Methods	Results
1.	Mc Mahon et al., 2014	Assess dysfunctional taste and explore the relationship of dietary sodium intake with taste disturbance.	91 adult CKD stage 3-5 (78% male) aged 65.9 ± 13.5 years, eGFR of 33.1, and 30 controls (47% male) aged 55.2 ± 7.4 years. Cross-sectional. Analysis: chi-square (differences), t test (intensity) and multivariate (age and gender)	Identification and intensity of salty taste were impaired in CKD compared with controls. Taste changes occur with CKD, independent of age and gender differences, with specific impairment in salty tastes
2	Manley et al., 2015	The genetic ability to taste bitter, in CKD patient's saliva, impacts on the uremic upper GI symptoms experienced	56 CKD patients (35 males, 21 females, age 67 ± 14 years), with CKD stages 4 and 5. Cross-sectional study. Analysis: descriptively and regression correlation	Reported 29 (52%) major upper GI uremic symptoms, whereas 27 (48%) had no symptoms or only minor complaints of dry mouth. There was a strong association between the genetic ability to taste thiourea (bitter).
3	Shim et al., 2016	Relationship between sodium intake and Salty taste thresholds preference	118 healthy young women. Cross sectional. Analysis: descriptively and Spearman correlation	Salty taste preference positive correlation with daily Sodium intake and sodium intake-increasing behaviors Detection and recognition threshold of salty taste no association with salty preference, sodium-related dietary behaviors, and sodium intake.
4	Giugno et al., 2017	Taste distortion in patients with (CKD	104 subjects with CKD. Cross-sectional. Analysis: descriptively	Taste distortion questionnaire. 28.7% of respondents had a loss of taste (96.60%) CKD patients
5	Konstantinova D, et al., 2017	Taste disorders in patients with end-stage kidney disease.	104 patients. A control group and a study group. The data was collected through a questionnaire. Analysis: SPSS (epidemiology and clinical), chi-square (non-parametrics)	28.7% of respondents had a loss of taste (96.60% CKD patients). Significant correlation between the duration of treatment and taste loss, age, and taste impairment, and between patients' age and the sense of a metallic taste. Distortion is an oral manifestation characteristic of CKD patients.
6	Tanaka et al., 2019	Salt taste threshold was measured among HD patients	99 maintenance HD patients. Cross-sectional. Analysis: descriptively and Spearman correlation.	The prevalence of salt taste dysfunction was more than 50% among HD patients., and many patients also had heterogeusia and ageusia. No significant association between salt taste dysfunction and IDWG.
7	Fitzgerald, 2019	Characterize altered taste perceptions in patients on dialysis compared with healthy adults, and to evaluate relationships between serum parameters with taste perceptions.	17 CKD patients were compared with 29 controls with normal gustatory function. Analysis: descriptively	Greater dietary sodium intake is associated with higher blood pressure, greater IDWG and greater all-cause mortality on a population-wide basis in chronic HD patients.
8	Kim et al., 2018	Salty taste thresholds and preference in patients with CKD according to disease stage.	436 patients with non-dialyzed CKD (stage 3, 4, 5) and 74 normal controls. Cross-sectional. Analysis: descriptively	Detection and recognition of taste thresholds of the stage 3 CKD patients > controls. Salty taste preferences of stage 5 and salt usage behavior scores of stages 4 and 5 CKD patients < normal controls.

(Continued)

Table 2. Factors Influenced Taste Disorders/Dysgeusia in Chronic Kidney Disease (Continued)

No	Author	Aim of the Study	Participants and Methods	Results
9	Ahn et al., 2019	Comparing the effect of decreasing eGFR due to salt intake between the intensive low-salt diet education group against the education conventional program	171 participants, case controlled. Analysis: descriptively	An intensive low-salt diet education program reduced the rate of decline in kidney function in hypertensive CKD patients regardless of its effect on decreased salt intake or albuminuria during 36 months of follow-up.
10	Wright et al., 2019	Applying the Theory of Planned Behavior (TPB) framework	63 subjects non-dialyzed CKD. Cross sectional. Analysis: descriptively	TPB successfully identified barriers or key contributing factors (Taste preferences, willpower, meeting social expectations, and disease concern) to follow a low-sodium diet in non-dialyzed people with CKD.
11	Vengalasetti et al., 2021	Determine the independent associations among CKD, CKD stage, and dysgeusia and dysosmia	Data from the National Health and Nutrition Examination Survey (NHANES) years 2011-14. Case control. Analysis: multivariable logistic regression	Non-dialysis-requiring CKD is significantly associated with self-reported dysgeusia.
12	Melilo et al., 2021	Observation and analysis of correlation between longer CKD duration (stage of CKD) with taste dysfunction	100 CKD age 19-86 year and 100 controls age 20-85. Case control. Analysis: Descriptively and Chi square	Hypogeusia in CKD were 27% dysfunction The duration of CKD>24 months was significant as a predictor of taste dysfunction [OR 4.889]. Stages of CKD had no relationship with the severity of taste dysfunction. No significant relationship between age and taste function score among patients with CKD
13	Chewcharat et al., 2022	The association between olfactory and gustatory dysfunction and CKD.	3527 US adults aged ≥40 years old in NHANES between 2013 and 2014. using the "scratch and sniff" NHANES Pocket Smell Test and quinine whole-mouth test. Cross-sectional. Analysis: Multivariable logistic regression (survey weights and design factors). multivariable linear regression, Wald F-test for continuous variables or chi-square tests for categorical variables (dysfunction).	The prevalence of olfactory dysfunction was 30% among CKD and 15% among non-CKD ($P < .001$). The prevalence of gustatory dysfunction was 13% among CKD and 17% among non-CKD ($P = .10$). CKD was significantly associated with olfactory dysfunction but not gustatory dysfunction.
14	Yusuf et al, 2022	Comparison between taste perception disorder for salt, sour, sweet and bitter in CKD and non-CKD patients in Nigeria	100 CKD and 100 controls. Age 18-69 year. Case control. Analysis: descriptively and Spearman correlation.	Hypogeusia in CKD was 27% dysfunction for salt, sour, sweet and bitter taste of 13.0, 24.0, 13.0, and 17.0%, respectively. Hypogeusia in Control only 1% for each of the taste modalities

CKD, chronic kidney disease; TPB, Theory of Planned Behavior

(Joo's, Tokuyama's, and Maruyama's studies). In Maruyama's[11] study, estimates of glomerular filtration rate(eGFR) was not independently associated with serum zinc levels; this may be due to confounding factors, such as nutritional status and degree of anemia. Serum albumin, hemoglobin, and mean corpuscular volume (MCV) were independently associated with serum zinc. Serum zinc levels tend to decrease with increasing stages of CKD ($P = .051$). Zinc deficiency is one risk factor for the development of CKD. In severe CKD conditions, hypoalbuminemia will occur, which will exacerbate the condition of zinc deficiency. This condition happens in a continuous vicious circle.

Zinc supplementation is not necessarily beneficial for all CKD patients, zinc is especially beneficial for those who are malnourished and anemic, according to Maruyama' study, for nutritional status in children and adolescents with CKD according to Escobedo-Monge' study.

Estimates of glomerular filtration rate (eGFR), sodium intake behavior scores, preference for salty taste, smoking, gender, and zinc levels were significantly associated with mean sodium urine spot in CKD subjects. Results of Kim's (2018) study showed that eGFR and salty taste preference were independently correlated with mean sodium urine spot.

Table 3. Effect of Zinc to CKD

No	Author	Aim of the study	Participants and Methods	Results
1	Kim et al., 2016	The effect of zinc deficiency on salt taste acuity, preference, and dietary sodium intake in HD patients.	77 HD patients. Cross-sectional. Analysis: descriptively and logistic correlation.	The mean salt recognition threshold and salty taste preference were significantly higher in the zinc-deficient group. Zinc deficiency may be related to low salt taste acuity and high salt preference, leading to high dietary sodium intake in HD patients.
2	Escobedo-Monge et al., 2019	Effects of zinc Supplementation on Nutritional Status in Children with CKD	7735 participants with normal renal function. Randomized Control Trial. Analysis: descriptively and non-paired t-test	Zinc supplementation may be beneficial for nutritional status in children and adolescents with CKD, especially with 30 mg/day of zinc Supplementation
3	Tavares et al., 2021	Evaluate the association between zinc plasma levels and sensory perception in patients with CKD.	21 non-dialyzed CKD patients. Cross-sectional. Analysis: descriptively and Pearson correlation	Zinc plasma levels were significantly lower in CKD patients compared with the control group. Reduced zinc plasma levels in non-dialyzed CKD patients may be associated with a lower perception of bitter, sour, and salty tastes.
4	Joo YS, 2021	Dietary zinc intake and incident chronic kidney disease.	7735 normal renal function participants. Longitudinal study. Analysis: Multivariate Cox hazard	Low dietary zinc intake may increase the risk of CKD development in individuals with normal renal function.
5	Tokuyama et al., 2021	Effect of zinc Deficiency on Chronic Kidney Disease Progression and effect modification by hypoalbuminemia.	312 subjects (160 low-zinc vs 152 high-zinc). Cohort study. Analysis: Various Cox proportional hazard models	The low-zinc group showed a higher risk of the primary outcome [adjusted hazard ratio 1.81 (95% confidence interval 1.02, 3.24)]. Zinc deficiency is a risk factor for CKD progression
6	Maruyama et al., 2021	Prevalence of zinc deficiency and relationship to renal function in Japan.	816 non-dialyzed CKD subjects. Cross-sectional. Analysis: Multiple regression	High prevalence of zinc deficiency among non-dialyzed Japanese subjects. eGFR was not independently associated with serum zinc, probably due to confounding factors, such as nutritional status and degree of anemia.

CKD, chronic kidney disease; HD, hemodialysis

Effects of sodium on CKD: According to Meng's study, high salt intake approves increased both SBP and DBP, both in CKD and in healthy subjects. However, an increase in blood pressure is more in patients with already established hypertension. The study also shows that high sodium intake increases the mortality of CKD dialysis subjects. Increased sodium intake has proven directly to cause decreased kidney function both in the CKD andhealthy subjects according to Sugiura's, Koo's, and Swift's studies.

Salt intake, salty food preferences, and salt eating related habits are not related to the threshold of detection and introduction of salty taste. The Swift 2022 study and 2017 Advice stated that limiting salt intake would be very beneficial for health, especially in preventing an increase in blood pressure, maintaining hydration status, and improving proteinuria. According to Koh et al.,(2018) sodium restriction of 20 mmol/day in subjects with an estimated sodium intake of >150 mmol/day showed a reduction in BP and proteinuria.

There was aldosterone dysregulation in the CKD group in response to chronic salt administration, but dysregulation did not occur in the low sodium diet or acute sodium administration. Thus, Taylor et al.,(2018) suggested to CKD patients to always limit sodium intake but still take drugs prescribed by doctors.

The overall interrelationships and interactions between sodium intake, taste disturbances, zinc, and CKD are shown in Figure 2.

DISCUSSION

Sodium intake has two opposing effects in patients with CKD adverse and beneficial effects. The detrimental effect is that it escalates the mortality rate due to the increasing proteinuria and blood pressure, whereas the beneficial effect is that it improves the nutritional status as it improves appetite since salt contained in the food affects the taste of the food itself. Sodium intake is highly related to water intake via the thirst center. Thus, sodium intake affects the extracellular fluid volume, blood pressure, appetite, nutritional status, and mortality.[12]

Saltiness is a highly addictive flavour, and eating foods high in sodium will drive the desire to consume salty taste even more. Salty taste has the most important role related to salt

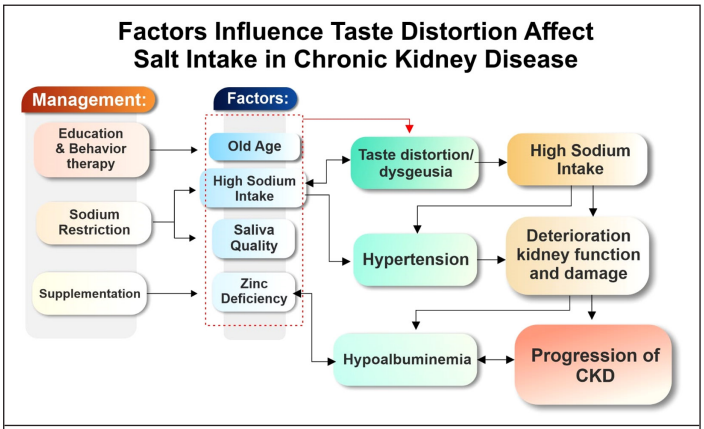

Figure 2. Schematic results from factors influence taste disorders affect sodium intake in Chronic Kidney Disease.

consumption in HD patients and is closely related to blood pressure, volume status, and prognosis. High sodium consumption is influenced by many factors, like habitual, culture, available natural sources, and taste perception disturbance.[13]

Many factors cause impaired taste perception: sodium intake, saliva, zinc status, age, race/genetic, comorbid diseases, and medications taken.[14,15] In this study, there were surmount suggestions for four factors that cause taste distortion in CKD: old age, salt intake, saliva quality, and zinc deficiency.

Chronic kidney disease patients have fewer fungiform taste buds than those without kidney failure, due to diabetic or uremic disease.[14] The study made by Taylor et al, results in a contradiction to their hypothesis. Turns out that CKD patients respond well to a low sodium diet short term (acute), and the physiological response of aldosterone secretion can be maintained normally.[16] Angiotensin-II stimulation caused comparable blood pressure and aldosterone responses in both control and CKD groups. According to the results of Taylor's (2018) study, aldosterone dysregulation occurred in the CKD group on long-term high sodium administration but did not occur with dietary salt modification (short term). Therefore, in patients with CKD, it is still recommended to restrict sodium intake along with continuing the drugs prescribed by physicians. Several studies have shown that aldosterone plays a direct role in kidney disease through an inflammatory process, fibrosis, and tissue necrosis. The use of aldosterone antagonists can increase the life expectancy of patients with CKD.[16]

In non-dialysis CKD patients, the perception of salty taste significantly correlated with urinary sodium excretion (UNA).[17] For CKD patients, the sensitivity or detection of salty taste decreases, which in turn causes higher oral salt intake to cause increased blood pressure.[18] An article by Galletti and Strazullo stated the results of the INTERSALT, an international study of electrolyte excretion and blood pressure epidemiological, that blood pressure increases along with age and was influenced by sodium intake.[5,18,19] High sodium intake is a risk factor for hypertension which is associated with the risk of kidney disease. This condition occurs due to an increase in angiotensin II and aldosterone release influence increasing blood pressure,[16] blood pressure response to increased salt intake is different and varies due to metabolic, neurohormonal factors, and genetic variations effects. Increased sensitivity to sodium can influence the development of organ damage independently.[19]

Increased salt intake can be caused by impaired taste detection or dysgeusia. This condition can occur both in CKD subjects, as well as in normal subjects. Shim et al. (2016) conducted a study on normal subjects, and it showed the total of normal people who experience taste dysfunction is quite large. More than a third of Shim's research subjects, around 42.1% of normal young adult women, had taste dysfunction (distortion) or hypogeusia towards salty tastes. Women are born with more taste buds than men (35% women,15% men), and this decreases after menopause. For researchers, it is important to consider gender differences when studying taste acuity.[20]

In the results of Shim et al.'s research, salty taste preference was positively correlated with a daily intake of dishes containing high sodium and a high intake of salt. The food preference description of how a person determines their food choices. Someone who prefers a salty taste is likely to choose foods with a saltier taste, while foods with a salty taste are likely to contain high sodium.

The results of research from Mc Mahon et al., Manley et al., Kim et al., Giugno et al., Tanaka Fitzgerald et al., and Velangasetti et al. strengthen the evidence which states that most CKD patients in general, both non-dialysis and dialysis patients, experience taste dysfunction, especially to the salty taste, which in turn cause increasing of sodium intake and 24-hour urine excretion and eventually can exacerbate kidney damage. In the study by Tanaka et al. (2019), there was no relationship between salty taste dysfunction and intra-dialytic weight gain (IDWG). The IDWG is the mean value of weight gain at the start of each week during one month of dialysis. In hemodialysis (HD) patients, according to Meng's study, the taste receptor for salt has the most important role related to sodium intake because it is associated with blood pressure, fluid volume status, and disease prognosis. According to Fitzgerald et al., an increase in dietary sodium intake will lead to an increase in blood pressure, IDWG, and an escalation in all-cause mortality in the population with HD. The IDWG describes weight gain due to water accumulation from metabolism, dietary sodium, and volume intake between dialysis sessions.[21,22] The results of Fitzgerald's study differ from the results of Tanaka et al., which states there is no significant relationship between salt taste dysfunction and IDWG. Perhaps there was a different response to each research subject. For example, some patients remain asymptomatic even though they have reached stage 5 CKD with eGFR <10 ml/min, whereas uremic symptoms usually appear when the creatinine clearance falls, and plasma urea increases.[22] Vengalasetti et al. examined dysgeusia and dysosmia occurring in CKD subjects. Impaired taste and smell

Table 4. Effects of Sodium on CKD

No	Author	Aim of the study	Participants and Methods	Results
1	Meng et al., 2014	Relationship between salt intake and SBP.	130 non-dialysis patients with CKD. Cross-sectional. Analysis: Multi-stepwise regression	The linear relationship between salt intake and SBP in non-dialysis patients with CKD. The salt sensitivity of BP rose with the decline of kidney function.
2	Koo et al., 2014	Association between 24-hr urinary sodium (24UNA) and adequacy of BP control in patients with CKD and non-CKD	400 subjects were sub-grouped by the amount of 24UNA or CKD stage. Cross-sectional. Analysis: chi-square and non-paired t-test	The difference in the amount of 24UNA between CKD and non-CKD except for each stage of CKD group. Salt intake is a risk factor in achieving appropriate BP control.
3	Oh et al., 2016	Investigate the relationship between blood pressure and salt consumption	19,476 participants in the 2009-2011 Korean National Health and Nutritional Examination Survey (KNHANES). Analysis: Descriptively and multiple regression	Increases in 24HUNa of 100 m Eq/day were associated with increased systolic/diastolic blood pressure. The effect was stronger in hypertensive participants and smaller in normotensive participants
4	Saran et al., 2017	Evaluate the effect of a sodium-restricted diet (SRD) versus usual diet on BP	58 adults with stage 3-4 CKD. Cross-sectional. Analysis: Non-paired t-test (cross-over)	Implementation of SRD in CKD stage 3-4 patients resulted in clinically and statistically significant improvement in BP and hydration status.
5	Koh et al., 2018	Predicting potential antihypertensive effect with dietary salt reduction of CKD subjects.	75 hypertensive patients with CKD. Longitudinal study. Analysis: Microsoft Excel and SPSS 15.0. Natural log to achieve the Gaussian distribution, and pair t-test	Salt restriction reduces BP, especially in patients with an estimated daily sodium intake of >150mmol/day. Reduction in sodium intake beyond 20 mmol/day reduced both BP and proteinuria.
6	Sugiura et al., 2018	Dietary salt intake as a deterioration predictor of kidney function in the general population.	12.126 subjects with a normal eGFR ≥60. Cross-sectional. Analysis: Multivariate Cox hazard and linear regression	The incidence of impaired kidney function in the normal population was higher in the group with high salt intake than low (P <.001).
7	Taylor et al., 2018	Relationships between salt intake, BP, and renin-angiotensin system in CKD.	12 CKD, 15 control. Case-control. Analysis: Descriptively	Dysregulation of aldosterone in CKD in response to salt loading with intravenous saline (long term), but not to dietary salt modification (short term).
8	Swift et al., 2022	Associations of sodium and potassium intake with chronic kidney disease in Study/Study of Latinos, 2008-2017.	Hispanic Community 9778 participants aged 18-74 yrs. Cohort study. Analysis: multivariable survey-weighted Poisson regression	Diets low in potassium and high in sodium are associated with an increased risk of developing CKD among healthy US Hispanic/ Latino adults

CKD, chronic kidney disease

perception may be associated with fluid imbalance, toxin accumulation, and impaired metabolism of kidney disease.[14,23] Impaired taste perception and digestive tract problems are common in CKD, with incidence ranging from 31% to 81% (according to Manley and another study).[14,23] Fitzgerald 2019 study found that in a dialysis population in Lafayette, Louisiana, USA, about 43.8% suffered from impaired taste perception. Some possible causes of taste dysfunction in CKD include intraoral dryness due to water loss, peripheral nerve disorders due to uremia and diabetes, drug-related side effects, and zinc deficiency; however, the exact mechanism is not yet fully understood.[15,24] The deficiency of vitamin B12 has a clear effect on taste perception disorder as it disrupts epithelial cells, producing tongue pain, redness of the tongue, and the absence of papilla, thereby increasing taste.[25] Vitamin B12 not only acts as a cofactor in homocysteine metabolism; however, it likely has a direct effect in causing tissue damage and cardiovascular risk in CKD and ESRD.[26]

Taste recognition in the oral cavity is influenced by saliva. Saliva aids taste perception in the transport of taste substances, the solubility of substances, and protects taste receptors from damage caused by dryness, disuse atrophy, or infection.[27] Normal saliva is hypotonic, high in potassium and phosphorus but low in sodiumand urea. The only food or liquid that cannot be interpreted by the human brain is saliva itself due to the familiarization of taste.[28]

Interesting facts show that the saliva of CKD patients is different from that of normal subjects, while it proves that the ability to taste flavors is influenced by saliva. The ability to taste in CKD patients is influenced by the characteristics of saliva which genetically can have an impact on GI uremic symptoms, according to Manley's study. Results showed that in patients with taste dysfunction, changes in saliva composition are found to increase in active compounds, such as potassium, bicarbonate, and urea.[14,24] It is necessary to assess whether this taste perception abnormality has been present for a long time (genetic) or recently (due to CKD). Some people are born with taste buds that are more effective and can intensify taste recognition.[27] The saliva of patients with CKD generally has higher urea, sodium, potassium, phosphate, and pH levels than those without CKD, with taste and smell dysfunctions.[14,24]

Another cause of poor taste perception is low zinc plasma levels. The study by Tavares et al. showed plasma zinc levels in CKD patients were significantly lower than those in the control group.[29] Disruption in salty taste perception in zinc deficiency will increase sodium intake, which in turn causes kidney problems. The study made by Kim et al. involved CKD patients with HD, which showed a higher mean sodium recognition threshold and preference for salty taste in the zinc-deficient group compared to the non-deficient group. Deficiency or low zinc intake has proven to increase the risk of developing CKD, both in general people (Joo et al.'s 2021 study) and in CKD patients (Tokuyama et al.'s study). Serum zinc levels tend to decrease kidney function with increasing stages of CKD. One of the causes of zinc deficiency in CKD patients is low protein intake because zinc is abundant in protein. The phytate content of foods such as whole wheat and soy products is known to inhibit the absorption of zinc.[30,31] Low energy and/or protein intake can be followed by a decrease in nutritional parameters including hypoalbuminemia and increased risk of morbidity and mortality in patients with advanced CKD.[30] According to Maruyama's 2021 study, hypoalbuminemia, and lack of intake of protein will lead to zinc deficiency, which in turn leads to the worsening of CKD. About 80% of serum zinc is bound to albumin, and serum zinc and albumin levels were positively correlated. Guidelines to the Japanese Society of Clinical Nutrition, the limit value for serum zinc levels is 60 g/dL.[31] Zinc supplements may be beneficial for nutritional status in children and adolescents with CKD at a dose of 30 mg/day (Escobedo-Monge' study). Absorption of zinc in humans could be better by supplementation of zinc with picolinic acid. Zinc picolinate can be absorbed better than zinc gluconate, zinc citrate, or zinc oxide.[32]

These four factors (age, salt intake, saliva, and zinc deficiency) that affect taste perception are reciprocally associated with taste disorders, thus causing decreased eGFR due to increased sodiumintake, or can be directly related to worsening CKD. The way to break this chain of relationships is to reduce the influenced factors.[14,33] Manley (2014)[34] states that high sodium consumption (this condition cause taste disturbances in turn), and salivary composition can be surmounted by reducing salt intake. Zinc status can be improved by supplementation in the zinc deficiency conditions. According to Wright (2019), age is a factor that cannot change, but in the elderly, its effects can be overcome with education and good behavior planning.

Education of healthy food preferences to CKD patients through various strategies and programs to reduce their sodium intake is very necessary. Kim et al. (2018) stated adequate education for CKD patients to change taste preferences is important to reduce sodiumin take. In a study conducted by Ahn et al., an intensive education program on a low sodium diet for 36 months succeeded in inhibiting the decline in kidney function in patients with CKD hypertension.[35] Wright et al., by applying the Theory of Planned Behavior (TPB) identify factors that contribute to dietary adherence tosodium restriction are taste preferences, willpower, social expectations, and concern for disease. These factors need to be considered to succeed sodium restriction diet.[36]

Excessive salt intake can cause hypertension which will lead to CKD but can also directly cause worsening of kidney function and this will lead to worsening of CKD. McCausland et al. (2012) argue that increases in dietarysodium can escalate mortality among HD patients. On the other hand, too low sodium restriction especially in HD patients will increase the risk of death. During peritoneal dialysis, it is proven that dietary sodium that is too low increases the risk of death.[22] One of the explanations is that sodium and calorie intake are highly correlated.[14,15] McCausland's study and Saran's study suggested adequate soidum intake is 2000 (IQR 2000-3000) mg/day. According to Koh's study 2018, reduction of soidum intake by more than 20 mmol/day = 0.46 g = 1.16 g salt has proven to reduce both blood pressure and proteinuria. Sodium restriction is effective in lowering blood pressure, especially in patients with an estimated daily sodium intake of >150 mmol/day = 3.45 g Na or 8.7 g salt. Conversely, excessive sodium intake will cause an increase in SBP, especially in patients with decreased kidney function (Meng et al.'s study 2014), as well as in patients with hypertension (Oh et al.'s study 2014). Meanwhile, contrary to the general population's opinion, high sodium intake greatly affects the decline in kidney function, regardless of its effect on blood pressure. Very high sodium diets not only decrease eGFR but cause kidney fibrosis and hypertension. This has been proved in hypertensive and normotensive animal models (mice).[37]

Reduction of salt intake should be carried out not only by CKD patients, but by non-CKD as well. Sodium restriction is highly recommended for both the general population and patients with CKD because it can help to prevent the decline in kidney function and control blood pressure.

CONCLUSION

Many factors influence the intake of sodium and impaired taste perception. This study discusses the three most significant

factors that affect taste distortion: salt intake, saliva quality, and zinc deficiency, besides age. The conclusion of this study is tasting disorders in CKD are strongly influenced by high intake sodium, saliva, and zinc deficiency.

Taste disorders and detection in the CKD subject group are significantly different from the non-CKD subject group, although there are occurrences also within the non-CKD subject group. In the elderly subject group, excessive soidum intake can be reduced by education and behavioral therapy. Restricting sodium intake can improve the habitually high salt consumption and the quality of saliva. The relationship between zinc and CKD mutually affects each other, where zinc deficiency exacerbates the CKD status while CKD itself aggravates the zinc deficiency by distorted taste detection that leads to higher protein consumption and further progresses to hypoalbuminemia. In some cases, a deficiency of zinc was effectively treated with zinc supplementation.

Excess sodium intake accelerates CKD progression directly and indirectly by causing hypertension. Patients with CKD and normal subjects were suggested to limit their sodium intake. A suggestion for CKD patients is to reduce their sodium intake to less than the recommended limit (2300 mg/d) along with continuing drugs recommended by physicians.

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