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PROGRAMA MULTIDISCIPLINARIO DE POSGRADO EN CIENCIAS AMBIENTALES

TESIS PARA OBTENER EL GRADO DE

MAESTRÍA EN CIENCIAS AMBIENTALES

EVALUACIÓN DE LA FUNCIÓN RENAL EN TRABAJADORES PRECARIOS EXPUESTOS A CONTAMINANTES NEFROTÓXICOS EN ESCENARIOS VULNERABLES DE LA ZONA METROPOLITANA DE SAN LUIS POTOSÍ

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Resumen

El objetivo del estudio fue evaluar la función renal en tres grupos de trabajadores precarios (recicladores de basura, canteros y ladrilleros) de la zona metropolitana de San Luis Potosí. Se obtuvieron muestras de orina y sangre para la evaluación de parámetros clínicos como la creatinina sérica, la tasa de filtración glomerular y la albuminuria y la evaluación de metales pesados. También se evaluaron los marcadores de daño renal cistatina-C (Cys-C), osteopontina (OPN), β2-microglobulina (β2-MG), molécula de lesión renal-1 (KIM-1) y lipocalina asociada a gelatinasa de neutrófilos (NGAL) mediante el ensayo de cribado magnético humano personalizado luminex®. Se detectó exposición a V, Cr, Mo, Zn, Hg, As y Al. El escenario REC mostró las mayores concentraciones de cromo (36.03 ± 27.2 µg/l) en comparación con los escenarios CAN y LAD (8 ± 9.6 – 3.9 ± 6.6 µg/l, respectivamente $p<0.0001$). Asimismo, las concentraciones de mercurio resultaron ser superiores en el escenario LAD (3.7 ± 0.8 µg/l) con respecto a REC y CAN (0.7 ± 0.1 – 0.7 ± 0.0 ± 0.0 µg/l, respectivamente $p<0.05$). Por último, los escenarios CAN y REC mostraron una mayor concentración de As (25.4 ± 26.2 y 19.09 ± 16.7 µg/l, respectivamente) y en el caso del escenario LAD, las concentraciones de mercurio fueron superiores (3.7 ± 0.8 µg/l). En cuanto a los biomarcadores renales, las concentraciones de B2-MG fueron mayores en el escenario REC (87867± 115159.5 ng/g UCr) en comparación con los escenarios CAN y LAD (13649.9 ± 18314.5–10814.9 ± 15410.4 ng/g UCr $p<0.05$). Del mismo modo, la molécula Cys-C se observó en mayor concentración en el escenario REC (32795.61 ± 34965.8 ng/g UCr) respecto a CAN y LAD (5134.7 ± 11111.02–3957.7 ± 6488.5 ng/g Ir $p<0.05$). Los datos indican que los trabajadores en condiciones laborales precarias están expuestos a metales pesados y presentan altos niveles de proteínas en orina que favorecen el daño renal.

Palabras clave: Biomarcador renal temprano; Enfermedad Renal Crónica; Trabajo Precario; Nefrotóxicos; Metales Pesados.

Abstract

The study aimed to evaluate renal function in three groups of precarious workers (garbage recyclers, stonemasons, and brickmakers) in the metropolitan area of San Luis Potosí. Urine and blood samples were obtained to evaluate clinical parameters and metals by ICP-MS. The kidney damage markers cystatin-C (Cys-C), osteopontin (OPN), β2-microglobulin (β2-MG), kidney injury molecule-1 (KIM-1), and neutrophil gelatinase-associated lipocalin (NGAL) were also evaluated by luminex® custom human magnetic screening assay. Exposure to V, Cr, Mo, Zn, Hg, As, and Al was detected. The REC scenario showed the highest chromium concentrations (36.03 ± 27.2 µg/l) compared to the CAN and LAD scenarios (8 ± 9.6 - 3.9 ± 6.6 µg/l, respectively $p<0.0001$). Likewise, mercury concentrations were higher in the LAD scenario (3.7 ± 0.8 µg/l) compared to REC and CAN (0.7 ± 0.1–0.7 ± 0.0 ± 0.0 ± 0.0 µg/l, respectively $p<0.05$). Finally, the CAN and REC scenarios showed higher As concentrations (25.4 ± 26.2 and 19.09 ± 16.7 µg/l, respectively), and in the case of the LAD scenario, mercury concentrations were higher (3.7 ± 0.8 µg/l). Regarding renal biomarkers, B2-MG concentrations were higher in the REC scenario (87867± 115159.5 ng/g UCr) compared to the CAN and LAD scenarios (13649.9 ± 18314.5 - 10814.9 ± 15410.4 ng/g UCr $p<0.05$). Similarly, the Cys-C molecule was observed in higher concentration in the REC scenario (32795.61 ± 34965.8 ng/g UCr) concerning CAN and LAD (5134.7 ± 11111.02 - 3957.7 ± 6488.5 ng/g UCr $p<0.05$). Data indicate that workers in precarious working conditions are exposed to heavy metals and present high levels of urine proteins that favor renal damage.

Keywords: Early Kidney Biomarkers; Chronic Renal Disease (CRD); Precarious work; Nephrotoxic; Heavy Metals.

Introducción general

De acuerdo con la Organización Internacional del Trabajo (OIT) y la Conferencia Internacional de Estadísticos del Trabajo (CIET), el trabajo informal lo define como aquellos trabajadores por cuenta propia; que no suelen tener contratos de trabajo explícitos y por escrito, y que por lo general el empleo no está sujeto a una legislación laboral y a reglamentos de seguridad social (1). De acuerdo con la Encuesta Nacional de Ocupación y Empleo (ENOE) en el segundo trimestre del 2022, el 55.2% de la población ocupada se encontraba en la informalidad, lo que representó a 32 millones de personas; teniendo un aumento de 985 mil personas con respecto al mismo lapso del año 2021 (2).

Bajo este enfoque, algunos de los empleos informales llegan a ser empleos precarios (3). La precarización laboral se ha relacionado a empleos de baja calidad con escasa seguridad y que coloca al trabajador en diferentes grados de inseguridad laboral y vulnerabilidad socioeconómica (1). De esta manera, la desatención de la salud de los trabajadores precarios llega a ser algo común que, aunada a sus actividades diarias de trabajo sin una capacitación de seguridad laboral y sin un equipo de protección adecuado, los puede exponer de manera crónica a mezclas de contaminantes tóxicos generados durante sus actividades. Esto representa un riesgo para la salud humana (4), ocasionando enfermedades que generan gastos catastróficos, tales como la Enfermedad Renal Crónica (ERC). La ERC se define como la presencia de una alteración a nivel estructural o funcional del riñón que persiste por más de tres meses (5). Estudios epidemiológicos han demostrado que existe una asociación entre contaminantes ambientales (nefrotóxicos) y la presencia de un daño renal crónico (6). Se ha atribuido alrededor de 14% de las muertes por ERC a la ocupación laboral por la exposición a sílice, solventes orgánicos, plomo y cadmio (7). Actualmente, esta enfermedad se ha transformado en un problema de salud pública mundial debido al número creciente de casos, así como a los altos costos de inversión en el tratamiento de la enfermedad, así como a la detección tardía (5). No obstante, la ERC puede ser revertida o postergada en sus etapas iniciales a través del control de la presión arterial, el manejo de la glucosa y colesterol, así como una adecuada dieta. Asimismo, el empleo de biomarcadores tempranos puede servir en la detección y diagnóstico temprano de una alteración a nivel renal, especialmente en trabajadores expuestos a contaminantes nefrotóxicos y que se encuentran laborando en escenarios de precariedad laboral.

Evaluation of renal function in precarious workers exposed to heavy metals in vulnerable scenarios in the metropolitan area of San Luis Potosí, México.

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ABSTRACT

The aim of the study was to evaluate renal function in three groups of precarious workers: garbage recyclers (REC), quarry workers (CAN), and brickmakers (LAD). Urine and blood samples were collected to evaluate clinical parameters and metal levels using ICP-MS. The REC group had the highest concentrations of chromium (36.03 ± 27.2 µg/l) compared to the CAN and LAD groups. Mercury concentrations were higher in the LAD group (3.7 ± 0.8 µg/l). Additionally, both CAN and REC groups had higher concentrations of arsenic (25.4 ± 26.2 and 19.09 ± 16.7 µg/l, respectively), while mercury concentrations in LAD (3.7 ± 0.8 µg/l). In kidney biomarkers, β2-microglobulin concentrations were higher in the REC group (87867± 115159.5 ng/g UCr). Similarly, cystatin-C concentrations were higher in the REC group (32795.61 ± 34965.8 ng/g UCr). The data suggests that precarious workers are exposed to heavy metals and have elevated protein levels, contributing to kidney damage.

Keywords

Early Kidney Biomarkers; Chronic Renal Disease (CRD); Precarious work; Heavy Metals

1. INTRODUCTION

According to the International Labor Organization (ILO), of the world's total employed population over 15 years of age, 2 billion people work in the informal economy, representing more than 61% of global employment (1). In Mexico, according to the National Occupation and Employment Survey (ENOE), in the first quarter of 2022, 55.2% of the employed population was in the informal sector, which represented 31 million people, an increase of 1.8 million people compared to the same period in 2021 (2). Under this approach, some informal jobs become precarious jobs (3).

Precarious employment has been recognized as a multidimensional concept ranging from job insecurity and low wages to limited social protection (4). This lack of economic stability, labor rights, and social security has distinguished precarious employment as a social determinant of poor health, affecting the worker, the family nucleus, and societies (5). Similarly, the literature has described a wide range of health problems related to precarious employment (6), including cardiovascular diseases (7), respiratory problems, allergies, and infectious diseases (8), as well as liver and kidney diseases (9)(10).

These health problems in workers have been directly related to their daily work activities. Dangerous conditions without occupational health and safety training and the lack of access to specialized health services can expose workers to chronic mixtures of toxic pollutants to human health (11). These include heavy metals (12) and polycyclic aromatic hydrocarbons (PAHs) (13), among others. Constant exposure to these toxins can lead to diseases that could generate catastrophic costs, such as chronic kidney disease (CKD).

Scientific evidence shows the relationship environmental pollutants and chronic kidney damage (14) (15). Epidemiological studies have shown that about 14% of deaths from CKD have been attributed to occupational exposure to silica, organic solvents, lead, and cadmium (16). Consequently, renal lesions are a worrying problem for health due to the difficulties in their prediction and diagnosis. CKD has become a public health difficulty due to the increasing number of cases, high investment costs, and late detection (17). Currently, 850 million people worldwide are affected by kidney disease (18). In Mexico, a prevalence of CKD of 12.2% was reported (19), and 12.75 deaths per 100,000 inhabitants (20). The diagnosis of this disease is made through blood urea and serum creatinine (sCr) levels; however, studies have shown that these levels lack a high predictive level (21) because serum creatinine concentrations increase in serum only when approximately 40–50% of the renal parenchymal is reversibly or irreversibly damaged (22). For this reason, this may lead to a lack of timely detection of early stages of acute or chronic renal failure. Nevertheless, kidney injury molecule-1 (KIM-1), cystatin-C (Cys-C), osteopontin (OPN), 2-microglobulin (2-MG), and lipocalin associated with neutrophil gelatinase (NGAL), have been shown to be more sensitive than sCr. These biomarkers are more sensitive than sCr, detecting specific tubular and glomerular damage. For this reason, these renal biomarkers can help detect and diagnose an alteration at the renal level, especially in workers exposed to nephrotoxic contaminants and working in precarious labor scenarios. This allows the establishment of health surveillance for the timely detection of this disease.

In San Luis Potosí there are clear examples of these scenarios, such as the garbage recyclers in Milpillas, the stonemasons in Escalerillas and the brickmakers in the Tercera Chica neighborhood. These scenarios are characterized by precarious working conditions, marginalization and exposure to contaminants and are therefore under constant chemical, physical and biological threats.

The study's main objective was to evaluate renal function in precarious workers exposed to nephrotoxic contaminants through biomarkers of early renal damage in vulnerable scenarios in the metropolitan area of San Luis Potosí.

2. METHODS

2.1 Study design

Three marginalized scenarios were considered for this study: Milpillas, Escalerillas, and Tercera Chica, located on the outskirts of the city of San Luis Potosí and characterized by precarious working conditions. In addition to economic income that does not cover a person's basic needs (24). Similarly, it is important to emphasize that this population in the three sites is constantly exposed to various occupational contaminants that could be nephrotoxic (13).

Garbage recyclers (REC): The first area studied was the community of Milpillas, with coordinates 22° 15' 05" north latitude and 101° 07' 38" west longitude. It has a population of 1546 inhabitants and is considered a locality with a high degree of marginalization according to INEGI's Unique Catalog of Geostatistical Area Keys. In this place, garbage recycling is characterized as its main economic activity. Among their occupations, the search for materials of interest in the landfills is an unhealthy occupation due to the different chemical and biological threats. In addition, these workers collect different types of waste, including electronic waste, for subsequent burning to obtain copper for sale. During the burning of electronic waste, workers are exposed to various pollutants such as heavy metals, polycyclic aromatic hydrocarbons, and dioxin, among others (25)(26).

Quarry workers (CAN): The community of Escalerillas was chosen as the second site, with coordinates 22° 06' 46" north latitude and 101° 04' 46" west longitude. It has a population of 6226 inhabitants and is also considered to have a high degree of marginalization (27). The artisanal quarry workshop characterizes this locality as its primary economic income. It is worth mentioning that the raw material used is extracted from the area surrounding the community. The stone cutting and shaping process releases large amounts of compounds in the stones and minerals, such as silica dioxide (Si2O), and workers, without adequate protective equipment, could be exposed to these compounds.

Brick workers (LAD): The last study site is in the Tercera Chica neighborhood, with coordinates 22° 11' 20" north latitude and 100° 58' 10" west longitude. It is a locality with a high degree of marginalization (27) known as "Las Ladrilleras" due to the manufacture of handmade bricks. During the manufacturing process of this product, the kiln must be kept burning for at least 12 hours, causing workers to look for cheap fuel alternatives such as domestic and industrial waste. This leads to the release of various compounds into the environment, such as metals, volatile organic compounds, dioxins, particulate matter, and polycyclic aromatic hydrocarbons.

2.2 Study Participants

For selecting the study participants, the following inclusion criteria were used: workers over 18 years of age with a minimum of two years working in a precarious occupation, male or female, and with a signed consent form. On the other hand, as an elimination criterion, the biological samples were not considered impossible to handle.

2.3 Sample Collection

Before sample collection, each worker was asked to fast for at least 12 hours, not to drink alcoholic beverages or smoke, and not to perform physical exertion for at least 24 hours before the sample. During collection, biological samples were taken by trained personnel and under all biosafety measures. Urine samples were obtained from the first urination of the morning, deposited in sterile 100 mL bottles, and immediately stored at –20°C for preservation. On the other hand, peripheral blood samples were obtained by venipuncture using BD Vacutainer vacuum collection tubes with and without anticoagulants to get serum and whole blood, respectively. Finally, samples without anticoagulant were centrifuged at 1500 rpm for 10 minutes, and serum was collected from each sample.

2.4 Biochemical Analyzes

Glomerular filtration rate and albuminuria parameters were analyzed in the urine sample. The albumin/creatinine ratio (CAR) was analyzed using MultiCare TM with U-Albumin Test Kit (SD BIOSENSOR). On the other hand, serum creatinine was determined in the blood sample and estimated using a chemistry analyzer (Olympus Diagnostic GmbH, Hamburg, Germany). Finally, the estimated glomerular filtration rate (eGFR) was calculated using the CDK-EPI formula.

2.5 Renal damage biomarkers assessment

Through a urine aliquot, cystatin-C (Cys-C), osteopontin (OPN), 2-microglobulin (2-MG), kidney injury molecule-1 (KIM-1), and lipocalin associated with neutrophil gelatinase (NGAL) were assessed using a luminex® custom human magnetic screening assay. Renal biomarker concentrations were obtained using a Luminex xMAP® instrument (MAGPIX®, Luminex).

Measurements were performed following the manufacturer's instructions and based on their described methodology.

2.6 Determination of exposure to heavy metals in urine

Before analysis by inductively coupled plasma mass spectrometry (ICP-MS), urine samples were prepared by the microwave digestion method, diluted 1:3 with 10% HNO_3 and a mixture of internal standards of 7 heavy metals Vanadium (V), Chromium (Cr), Molybdenum (Mo), Zinc (Zn), Mercury (Hg), Arsenic (As), and Aluminum (Al) was added. The standard procedure suggested for urine samples was followed, consisting of three 5-minute power steps (250, 400, and 600 W). ICP-MS performed elemental analysis with the following instrument parameters: carrier gas flow rate, 0.80 L /min; auxiliary gas flow rate, 0.75 L /min; cooling airflow rate, 13 L /min; and radiofrequency power, 13 kW.

2.7 Statistical Analysis

The concentration of metals in biological samples was subjected to an ANOVA with a post-hoc Dunnett's test ($p<0.05$). Based on the exposure variables and renal biomarkers, a principal component analysis was performed after transformation ($y=\log(x+1)$) and normalization. An unrestricted PERMANOVA analysis was used to determine the difference between the scenarios evaluated. PRIMER 7.0 add-on software was used for multivariate analysis. Statistical difference at least $p<0.05$.

3. RESULTS

3.1 General characteristics of the study population

Table 1 describes the anthropometric characteristics of the population. The mean age of all workers evaluated was 44.07 ± 14.9 years, with a height of 1.7 ± 0.1 m and weight of 86 ± 18.2

kg (data not shown). The percentage of overweight and obesity based on BMI per scenario was evaluated. In this context, REC presented the highest percentage of overweight individuals (47%), followed by CAN and LAD (40% and 32%). On the other hand, CAN and LAD had similar percentages of people (60% and 54%, respectively) with obesity regarding recyclers (33%)

3.2 Biochemical Analyzes

The clinical data in Table 2 showed similar serum glucose levels for each scenario (94.27 ± 34.20, 100.4 ± 42.2 and 94.2 ± 25.8 mg/dl, $p<0.05$). On the other hand, REC presented the highest urine albuminuria level with a mean of 20.42 ± 42.46 mg/g Cr, followed by LAD and CAN (14.9 ± 25.1 and 12 ± 13.3 mg/g Cr, respectively). Finally, no statistically significant differences were found between the scenarios for glomerular filtration rate.

3.3 Determination of urinary concentration of heavy metals by ICP-MS

Table 3 shows the concentrations of heavy metals analyzed in urine. Exposure to vanadium (V), chromium (Cr), molybdenum (Mo), zinc (Zn), mercury (Hg), arsenic (As), and aluminum (Al) was found. However, the REC scenario showed the highest concentrations of chromium (36.03 ± 27.2 μg/l) compared to the CAN and LAD scenarios (8 ± 9.6–3.9 ± 6.6 μg/l $p<0.0001$). Likewise, mercury concentrations were found to be higher in the LAD scenario (3.7 ± 0.8 μg/l), being different concerning REC and CAN (0.7 ± 0.1–0.7 ± 0.0 μg/l $p<0.05$). Finally, the CAN scenario showed a higher concentration of As (25.4 ± 26.2 μg/l). For REC there was also a higher concentration of As (19.09 ± 16.7 μg/l) followed by zinc (490.2 ± 669.8 μg/l) and molybdenum (90.7 ± 62.77 μg/l) and for the LAD scenario mercury concentrations were higher (3.7 ± 0.8 μg/l), followed by arsenic (47.2 ± 30.8 μg/l) and zinc (587.9 ± 504.4 μg/l).

3.4 Biomarkers of early renal damage (NGAL, B2-MG, Cys-C, OPN and KIM-1)

Table 4 shows the concentrations of biomarkers of early kidney damage in the population. The results indicate that in the REC scenario, B2-MG concentrations were higher (87867± 115159.5 ng/g UCr) compared to the CAN and LAD scenarios (13649.9 ± 18314.5−10814.9 ± 15410.4 ng/g UCr p<0.05). Similarly, the Cys-C molecule was observed in higher concentration in the REC scenario (32795.61 ± 34965.8 ng/g UCr), being statistically significant with respect to CAN and LAD (5134.7 ± 11111.02–3957.7 ± 6488.5 ng/g UCr p<0.05).

A PCA was performed using the variables of exposure to metals and renal markers. Figure 1 shows the PCA with a total variation of 66.7% (PC1: 26.7%, PC2: 22.9%, PC3: 17.1%). The CAN and LAD scenarios show higher renal marker concentrations than REC. After PERMANOVA analysis, significant differences were found between CAN vs. REC (p<0.01) and LAD vs. REC (p<0.001) scenarios.

4. DISCUSSION

The different conditions in which people live and work generate social inequalities in health because not all social groups have the same possibilities of finding quality jobs; consequently, the population generates its jobs, which are temporary, lacking social benefits, with low salaries, and in dangerous working conditions (29). In this context, precarious labor in Mexico has been identified in marginalized areas and highly toxic scenarios (exposure to various pollutants), making workers more vulnerable to health problems. This study showed that, in the three scenarios evaluated, workers are in a high degree of marginalization, working more than 8 hours a day without any contract, and some people do not have social security.

In the annual World Employment and Social Outlook 2022, the International Labor Organization (ILO) reported that, in many developing countries, self-employment accounts for nearly 50% of employment.

In Mexico, approximately 32 million people are in the informal sector, representing 55.2% of the employed population and an increase of almost one million people regarding the same period in 2021 (2). This informality has become a structural problem in Mexico and many Latin American countries, representing more than 70% of net job creation since mid-2020 (30). According to research conducted in Mexico to evaluate the labor situation index, San Luis Potosí is above the average obtained (0.58), placing it in 12th place in the country, based on the working population present at least two factors: 1) employed in micro-businesses, 2) low income, 3) involuntary part-time work, 4) lack of benefits, 5) no permanent contract, 6) no unionization (31).

The concept of precarious work tends to be associated with deteriorating working conditions, providing an environment where the worker is unprotected and risks to physical safety and health (32). This is why precarious work is an important social determinant of health, representing a significant public health problem (33). In a study of urban workers in Peru, those working in the informal sector presented a higher prevalence of poor working conditions regarding safety, hygiene, and ergonomics than workers in the formal sector. This suggests that poor working conditions partly explain the negative effect observed on the health of informal workers. However, part of the effect could be related to other factors such as poverty, precarious living conditions, lack of access to health services, and the absence of social protection benefits. In another study from Central America, men who worked without social security coverage and were self-employed were likelier to report poor self-perceived health (35).

In addition, a study conducted in Brazil revealed that informal workers presented health problems such as arthritis, bronchitis, heart disease, cirrhosis, and chronic diseases more frequently than full-time workers with social protection (36).

In this sense, the health-disease process is in a stage of epidemiological transition in which infectious diseases and those related to situations of poverty continue to be important. Diseases such as diabetes, chronic kidney disease, cardiovascular diseases, and factors such as obesity, which have become a worldwide public health problem, are gaining strength. In addition, indirect evidence suggests an association between job insecurity (present in precarious workers) and high body mass indexes, BMI (38). In this study, BMI parameters were identified in the precarious working population, in which the average number of overweight people in the REC and CAN scenarios were above the average for adults in Mexico (36%) as opposed to LAD (32%). However, regarding the obesity index, REC was the lowest scenario with percentages of people (33%) below the national average (37%), but CAN and LAD were above (60% and 54%, respectively) (39). Regarding the increase in people with an index of overweight and obesity, Mexico has shown a nutritional transition recently, showing a change in the consumption of healthy foods for foods denser in energy, sugars, and fats. In addition, obesity has been shown to be more frequent in populations in vulnerable conditions. This is due to the coexistence of factors such as unemployment, high availability of foods with low nutritional content, low levels of food security, and limited access to health services. Similarly, obesity has been related to a higher prevalence of diabetes in adults and its complications (such as kidney disease). It has been recently proven that diabetes has been one of the diseases with the highest morbidity and mortality in Mexico, mainly due to the increasing rates of overweight and obesity. Similarly, indirect evidence suggests an association between job insecurity (present in precarious workers) and incident diabetes (41). This study strongly recommended that the incidence of diabetes in the study sites is above the national average (10.2%), although only the LAD scenario showed a lower percentage of workers (9%) (39). This represents a major problem in this type of scenario since it should be noted that 30% of diabetics are not treated, and 60% of those treated are found to have poor or inadequate controls.

Likewise, nearly 70% of people with diabetes die from cardiovascular complications, with nephropathy being 17 times more frequent in diabetics (42, 43). Due to the direct costs arising from the complications of this disease, it is often difficult to reduce or postpone them. Thus, a diabetic person in a situation of poverty and precarious employment will have 1) difficulty in obtaining an accurate diagnosis, adequate treatment, and access and 2) risk of more severe complications (43).

Diabetes mellitus, hypertension, and chronic glomerulonephritis are the main causes of chronic kidney disease (CKD) worldwide (44). However, it has been shown that environmental and occupational factors have recently been associated with this disease, especially in areas with socio-environmental vulnerabilities. Likewise, it has become a significant public health problem due to its high worldwide prevalence (13.4%) (45). In Mexico, for the year 2018, a prevalence of 12.4% was reported. Although its association with chronic diseases of higher prevalence in our country (diabetes and hypertension) is clearly described, it is essential to mention that it is a multifactorial disease. Precarious workers have several risk factors that can trigger this disease. For example, exposure to environmental pollutants such as some heavy metals is a significant factor in the development of kidney disease. This study showed exposure to 7 metals, such as V, Cr, Mo, Zn, Hg, As, and Al, which appear to be elevated by their concentrations. As was found above, the reference values in all three scenarios (27 μg/L) and Hg concentrations were found above the reference value in the LAD scenario (0.73 μg/L). A study conducted in informal e-waste recyclers demonstrated increased exposure to metals such as arsenic, chromium, mercury, and zinc due to workers recovering valuable components from electronics, including metals (47). On the other hand, mercury exposure has been reported to be high in workers who directly handle e-waste without adequate safety measures (48). It is common for the brick industry to use low-quality fuels, such as electronic waste and plastics, producing emissions of pollutants, including mercury (49). Therefore, the burning of these wastes and the lack of adequate protective equipment expose the working population to health risks (50). In addition, numerous epidemiological studies have shown evidence of renal lesions after acute and chronic exposure to various forms of Hg. Mercury accumulates easily in the kidney because the proximal tubule is the leading site of mercury species uptake and accumulation, inducing oxidative stress. On the other hand, a study on Saudi Arabian industrial workers showed that chronic exposure to Hg decreased renal expression of proteins involved in detoxification and reduction of oxidative stress (52).

The assessment of renal damage is determined with the albumin/creatinine ratio (CAR) and the estimated glomerular filtration rate (eGFR), which are considered traditional clinical markers. In this study, according to the KDIGO 2012, in the REC setting, 7% of workers were already in a G2A2 category2, representing a slightly decreased glomerular filtration rate and albuminuria level. However, symptoms of CKD are usually not evident in the early stages; therefore, biomarkers of early kidney damage, such as NGAL, KIM-1, Cys-C, OPN, and β2-MG, are currently used as early biomarkers (53)(54).

Several studies have reported altered levels of these biomarkers in patients with CKD-related diseases. In the case of NGAL, it is a lipocalin family protein released from the kidney's tubular cells when the effects of oxidative stress and cell apoptosis are diminished. The presence of this protein has been associated with exposure to different environmental pollutants, such as heavy metals (55). A study conducted on workers exposed to Al and Cr showed a significant relationship with increased concentrations of NGAL (56), suggesting that this molecule serves as a marker of toxicity related to environmental pollutants. The present study showed mean NGAL concentrations higher than those in similar studies (Table 6).

KIM-1 is a type of transmembrane glycoprotein that is expressed in proximal tubular cells. It has been described to have specific characteristics in the identification of nephrotoxic agents in the proximal tubule, such as Cd, As, and Pb (57). Similarly, increased urinary levels of KIM-1 have been observed in adults occupationally exposed to Hg (58). This study's mean concentrations were higher than those in other studies (Table 6), which may indicate a possible early renal injury related to toxic exposure.

Cys-C is a non-glycosylated protein (13 kDa) that is filtered into the blood through the glomerulus and reabsorbed in the proximal tubule completely; therefore, its presence in urine may indicate tubular damage and impairment (59). Concentrations of 3449 ng/g Cr have been detected in artisanal mercury mining workers and Cys-C values in adults with acute kidney damage (60). The concentrations found in our study were much higher, with a mean of 13962.66 ng/g Cr than other studies (Table 6). In that sense, studies have shown elevated urinary Cys-C concentrations as an indicator of renal tubular injury (60), demonstrating a relationship between this damage and factors such as diabetes, acute injury, and toxicity (61). So, it is still of interest for the results.

OPN is a glycoprotein that is expressed in various types of tissues, including the renal tubular epithelium. In the adult kidney, OPN is mainly expressed in the loop of Henle and has been considered a good predictor of CKD because its expression is involved in various pathophysiological processes (62) (63). It has also been used to evaluate early kidney damage in workers exposed to mixtures of contaminants (64)(65). Our study showed higher mean concentrations than similar studies in populations with various environmental toxics (Table 6). Thus, a higher urinary OPN level is a significant risk factor in the incidence of chronic kidney disease.

B2-MG is a low molecular weight protein usually filtered by the glomerulus and is reabsorbed and catabolized by proximal tubular cells. It is commonly used as an early marker of acute kidney injury (AKI) from various sources such as nephrotoxic exposure, elevated cadmium toxicity, after cardiac surgery, and other cardiovascular complications. In this study, mean concentrations of 37444.15 ng/g Cr were found, being lower compared to those of a study in workers exposed to Cd (148890 ng/g Cr) (Table 6). Its use has been limited because its stability depends on urine pH, degrading rapidly at room temperature and in acidic urine (pH <6) (54), so it could not be considered a reliable marker.

Finally, each scenario evaluated showed different exposure patterns due to the presence of some metals. For example, the presence of metals in the blood such as Ni (5.59 0.03 g/dl) and Cr (4.20 0.02 g/dl) (66) in a brickyard population like that of our study. Together with Al and As these metals were the ones that contributed most to the separation between scenarios. Some research has reported that these types of metals can be released from burning electronic machines, which are used as fuel for brick manufacturing in our study site. Likewise, pipping scenarios have shown lower exposure levels to these metals in urine (0.5 µg/l Ni, 4.10 µg/l Al, and 0.08 µg/l Cr, respectively) (67).

In addition to the above, renal biomarkers were increased in the three scenarios evaluated, which, according to the analyses shown, CAN and LAD shared similarities. Although there are no cohort values for the proteins evaluated for renal damage, the values reported showed elevated levels in other studies. Hence, detecting these molecules already represents a risk of renal damage. Despite not having found any association with exposure levels, it is important to mention that these types of workers are exposed to other pollutants, such as polycyclic aromatic hydrocarbons and volatile organic compounds, among others. Therefore, it is necessary to perform biomonitoring of different types of contaminants with nephrotoxic implications. The workers in the evaluated scenarios present a high risk of renal damage, so it is necessary to implement intervention strategies to improve their development in their activities based on the precautionary principle. In addition to the above, in San Luis Potosí, Mexico, the prevalence of kidney disease of unknown etiology has increased, in addition to the increase in urolithiasis associated with the extreme hardness of water used for human consumption. In this sense, the scenarios evaluated in this study are in marginalized areas that have led different population sectors to consume tap water, representing a risk for developing urolithiasis, a risk factor for CKD. Therefore, other strategies should be employed to reduce the risks of CKD, such as creating a risk communication program to avoid the consumption of tap water and the transition to decent work in marginalized brick sectors.

5. CONCLUSION

Our data indicate that workers in precarious working conditions are exposed to heavy metals and have protein levels that promote kidney damage. Therefore, the precarious working population should be considered vulnerable to health effects.

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TABLES

Table 1. General characteristics of the study population according to scenario.

	REC N=15	CAN N=15	LAD N=22
	Mean ± SD	**Mean ± SD**	**Mean ± SD**
Age (years)	43 ± 10	40 ± 12	48 ± 17
Height (m)	1.60 ± 0.06	1.68 ± 0.08	1.68 ± 0.07
Weight (kg)	72.25 ± 11.38	89.89 ± 20.04	87.81 ± 18.03
BMI kg/m2*	28.14 ± 4.01	31.75 ± 6.13	30.96 ± 5.59
Low weight (<18.5)	0%	0%	0%
Normal weight (18.5-24.9)	20%	0%	14%
Overweight (25-29.9)	47%	40%	32%
Obesity (>30)	33%	60%	54%

Data are expressed as mean and standard deviation. *BMI, body mass index, calculated by ranges proposed by the World Health Organization (WHO).

Table 2. Biochemical Analyzes

		REC		CAN		LAD	
	Reference Value (RV)	**Mean ± DE**	**%> RV**	**Result**	**%> RV**	**Result**	**%> RV**
Serum glucose (mg/dl)	**< 126**	94.27 ± 34.20	13%	100.4 ± 42.20	13%	94.23 ± 25.76	9%
HbA1c (%) *	**<5.6**	6.01 ± 2.18	27%	5.89 ± 2.28	20%	5.46 ± 1.59	9%
Serum Creatinine (mg/dl)	**0.7-1.3**	0.85 ± 0.21	13%	1.02 ± 0.13	0%	0.94 ± 0.15	0%
Urea (mg/dl)	**<40**	32.01 ± 12.86	20%	31.75 ± 5.63	7%	28.91 ± 6.66	5%
Glomerular Filtration Rate (ml/min/1.73m2) CKD-EPI	**90-120**	92.67 ± 16.24	47%	92.87 ± 15.48	47%	94.83 ± 16.33	27%
RAC (mg/g cre)	**<30**	20.42 ± 42.46	13%	11.95 ± 13.29	0%	14.86 ± 25.14	14%

Data are expressed as mean and standard deviation. *HbA1c: glycohemoglobin. RV: reference value. RAC, albumin creatinine ratio.

Table 3. Concentrations of heavy metals in the urine of the study population according to scenario.

		Mean ± DE	MIN	P25	P50	P75	MAX	RV	%>RV
REC	V	13.1 ± 7.9	0.00105	9.29	13.04	17.19	30.27		
	Cr	36.0 ± 27.18 [a]	4.97	15.14	26.65	52.03	90		
	Mo	90.7 ± 62.77	11.93	35.99	84.57	138.1	196.71	170	13%
	Zn	490.2 ± 669.8	0.63	123.03	246.96	446.42	2375	1100	13%
	Hg	0.7 ± 0.1 [b]	0.69	0.69	0.69	0.69	0.69	0.73	0%
	As	19.09 ± 16.7	0.03	7.32	12.87	27.48	58.32	27	27%
	Al	1000.7 ± 349.3	391.77	827.7	978	1207.05	1717.8		
		Mean ± DE	**MIN**	**P25**	**P50**	**P75**	**MAX**	**RV**	**%>RV**
CAN	V	12.8 ± 9.7	0.00105	3.2745	13.533	17.7705	31.845		
	Cr	8 ± 9.6 [b]	2.193	3.4515	4.911	7.8255	41.055		
	Mo	74.3 ± 37.7	32.196	46.5	54.951	95.265	168.75	170	0%
	Zn	460.9 ± 341.9	16.875	131.265	443.58	744.9	1010.1	1100	0%
	Hg	0.7 ± 0.0 [b]	0.6885	0.6885	0.6885	0.6885	0.6885	0.73	0%
	As	25.4 ± 26.2	2.121	8.5485	21.399	29.448	106.59	27	33%
	Al	419.6 ± 255.8	169.11	301.86	360.18	444.795	1270.5		
		Mean ± DE	**MIN**	**P25**	**P50**	**P75**	**MAX**	**RV**	**%>RV**
LAD	V	10.7 ± 6.8	0.00105	6.45675	10.5915	15.1005	23.436		
	Cr	3.9 ± 6.6 [b]	0.03195	0.03195	0.03195	5.79375	17.838		
	Mo	110.3 ± 191.6	2.823	36.4185	49.3185	95.4225	760.8	170	7%
	Zn	587.9 ± 504.4	213.33	316.5675	469.95	608.685	2190.3	1100	7%
	Hg	3.7 ± 0.8 [a]	2.88	3.051	3.3165	4.34775	5.217	0.73	100%
	As	47.2 ± 30.8	11.151	28.51275	40.7655	47.49825	129.9	27	78%
	Al	908 ± 966.5	204.48	398.76	510.915	918.3	3788.4		

All data shown for metal concentrations are in (µg/L). Mean, SD (Standard Deviation), P25, P50, and P75 (percentile) as µg/L.RV, reference value; &, Human biomonitoring reference values for metals and trace elements in urine derived from the Canadian Health Measures Survey 2007-2013. Min, Minimum; Max, Maximum. [a.b] Groups with different superscript letters are significantly different ($p<0.0001$)

Table 4. Kidney markers in urine

		Mean ± DE	MIN	P25	P50	P75	MAX
REC	B2-MG	87867 ± 115159.5 [a]	343.3	12940.1	32888.8	123367.8	337235.3
	NGAL	45028.42 ± 98158.9	1047.9	7526.2	9814.2	22628.6	386890.8
	OPN	1071878.98 ± 996922	84055.5	298778.1	758428.9	1887964.3	3212301.6
	KIM-1	284.49 ± 305.0	11.9	43.5	177.5	379.4	926.8
	Cys-C	32795.61 ± 34965.8 [a]	1139.4	8314.9	12360.7	57870.5	99154.0
		Mean ± DE	**MIN**	**P25**	**P50**	**P75**	**MAX**
CAN	B2-MG	13649.9 ± 18314.5 [b]	509.1	1903.1	4022.3	19560.4	60741.9
	NGAL	4608.2 ± 8247.9	149.0	407.8	857.1	5173.4	30533.2
	OPN	616541.9 ± 1100871.7	39988.4	82436.5	195251.2	706613.9	4370048.9
	KIM-1	827.7 ± 999.8	49.48	232.91	477.46	843.5	2535.3
	Cys-C	5134.7 ± 11111.02 [b]	160.9	656.4	2035.0	2911.1	43340.0
		Mean ± DE	**MIN**	**P25**	**P50**	**P75**	**MAX**
LAD	B2-MG	10814.9 ± 15410.4 [b]	170.3	1921.8	6761.0	9717.6	53447.9
	NGAL	3362.7 ± 4186.6	125.9	541.9	898.3	4084.3	14142.2
	OPN	497018.8 ± 675596.6	18416.9	92217.1	186930.5	660009.0	2922578.4
	KIM-1	181.1 ± 235.9	13.6	34.8	107.9	176.9	805.3
	Cys-C	3957.7 ± 6488.5 [b]	417.5	771.1	1454.6	3048.8	23151.3

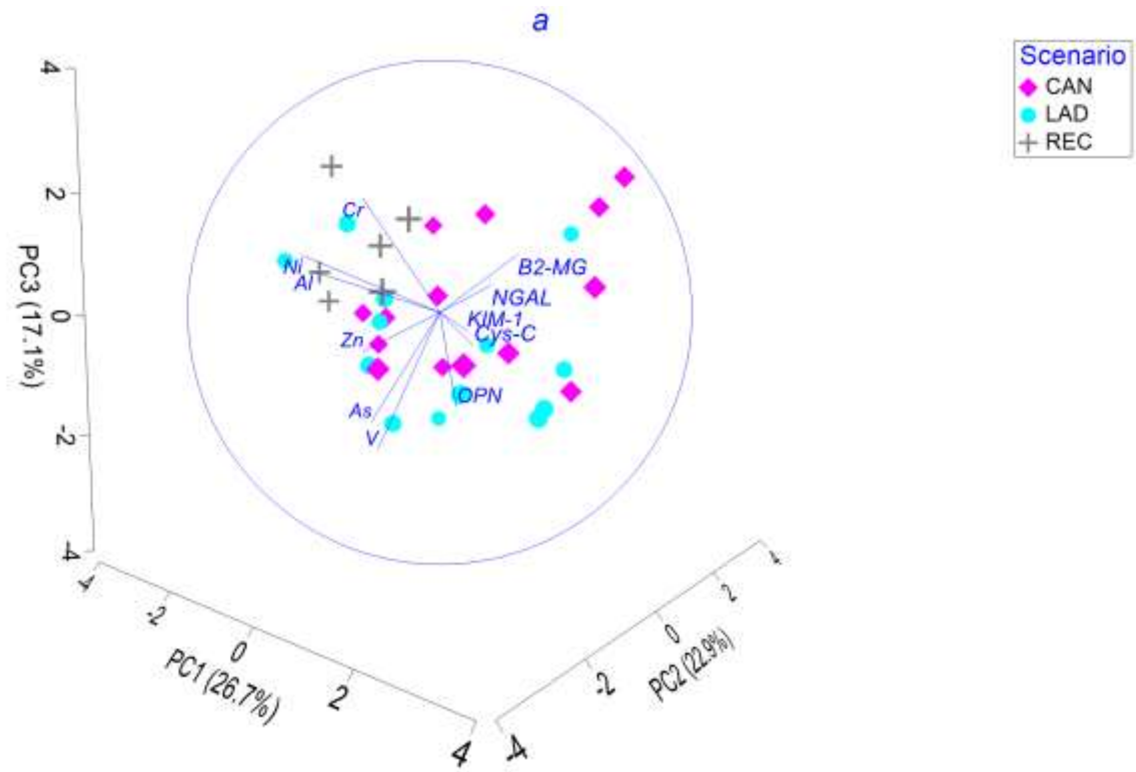
Abbreviations: B2-MG, betha2-migroglobulin; NGAL, lipocalin associated with neutrophil gelatinase; OPN, oteopontin; KIM-1, kidney damage molecule 1; Cys-C, cystatin-; SD. Standard deviation: P25, P50, and P75 (percentile) as ng/ g Cr. Biomarker concentrations in ng/ g Cr.

Table 5. Comparison of biomarker levels of renal damage with other studies.

B2-MG (ng/g Cr)	NGAL (ng/g Cr)	OPN (ng/g Cr)	KIM-1 (ng/g Cr)	Cys-C (ng/g Cr)	Referencia
-	2047	110971	23.89	3449	(58)*
-	12100	312300	-	12120	(61)$^+$
-	78.5	642.6	-	33.72	(68)$^+$
148890	-	-	-	-	(69)$^+$
87867	45028.42	1071878.98	284.49	32795.61	**REC**
13649.9	4608.2	616541.9	827.7	5134.7	**CAN**
10814.9	3362.7	497018.8	181.1	3957.7	**LAD**
37444.15	**17666.46**	**728479.91**	**431.10**	**13962.66**	**Mean**

*Data are shown as median and interquartile range. $^+$Data are shown as means.

Figure 1. Principal component analysis with renal biomarkers and metal exposure



CONCLUSIONES GENERALES

En conclusión, los resultados obtenidos a partir de este estudio revelan la presencia de un riesgo de desencadenar la enfermedad renal crónica en los trabajadores en los tres escenarios, especialmente en los recicladores de basura. Aunque no se establecieron valores de referencia específicos para las proteínas evaluadas, los niveles observados en comparación con otros estudios sugieren la urgencia de abordar esta problemática. Se encontraron altos niveles de metales pesados en la orina de los trabajadores, los cuales algunos están correlacionados con los biomarcadores renales.

Es esencial tener en cuenta la posible influencia de otros contaminantes a los que estos trabajadores están expuestos. Por ende, se recomienda llevar a cabo un biomonitoreo exhaustivo que incluya otros contaminantes con potenciales efectos nefrotóxicos. Además, la relación entre los escenarios evaluados y la creciente prevalencia de enfermedades renales en la región subraya la importancia de mejorar las condiciones laborales en comunidades marginadas.

Es fundamental un enfoque integral y multidisciplinario que aborde tanto los riesgos ocupacionales como el contexto social y ambiental de estas poblaciones de trabajadores.