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# CONCENTRAÇÕES DE RADÔNIO NA URINA E SORO DE PACIENTES COM CÁLCULO RENAL E INSUFICIÊNCIA RENAL

# CONCENTRATIONS OF RADON IN URINE AND SERUM OF PATIENTS WITH RENAL STONE AND RENAL FAILURE

# تركيز الرادون في البول والمصل لدى مرضى حصوات الكلى والفشل الكلوي

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## RESUMO

**Introdução:** Fontes naturais e artificiais de radiação afetam os seres humanos quando expostos a elas. Radionuclídeos emitem partículas alfa e beta, que podem interagir com os elétrons dos átomos circundantes de diferentes matérias, o que leva à ionização e destruição desses tecidos, podendo causar muitas doenças. A concentração de radiação no sangue e na urina aumenta, e uma das fontes mais perigosas de radiação disponível é o radônio. O**bjetivo:** Determinar a concentração de gás radônio ($^{222}Rn$) em amostras biológicas (urina e soro) usando um detector de traços nucleares de estado sólido (CR-39). **Métodos**: amostras biológicas (urina e soro) foram analisadas neste estudo na Província de Najaf, Iraque, de pacientes com cálculo renal, pacientes com insuficiência renal, pacientes com doença renal crônica e um grupo de pacientes controle saudáveis em três faixas etárias. **Resultados**: os níveis médios de $^{222}Rn$ em amostras de urina para controles saudáveis e pacientes com cálculos renais (17,27 e 22,77), os níveis médios de $^{222}Rn$ em amostras de soro para controles saudáveis, pacientes com cálculos renais, pacientes com insuficiência renal, pacientes com doença renal crônica (2,43, 9,83, 6,99 e 4,24) respectivamente. **Discussão**: verificou-se que os níveis de $^{222}Rn$ são mais elevados nas amostras de urina em comparação com o soro, e os níveis de $^{222}Rn$ no soro de todos os pacientes são mais elevados do que em pessoas saudáveis. Essas diferenças são estatisticamente significativas $p < 0{,}01$, o que indica que pacientes com cálculo renal e pacientes com insuficiência renal estão associados a um aumento significativo nos níveis de $^{222}Rn$ em comparação com pessoas saudáveis. **Conclusões**: os níveis de $^{222}Rn$ na urina e no soro podem ser considerados como um biomarcador para discriminar entre pacientes e indivíduos saudáveis. Os resultados deste estudo podem, portanto, ser usados como uma potencial ferramenta de diagnóstico para pacientes renais.

**Palavras-chave**: *cálculo renal, insuficiência renal, radônio.*

## ABSTRACT

**Background:** Natural and artificial sources of radiation affect humans when exposed to them. Radionuclides emit alpha and beta particles, which can interact with the electrons of the surrounding atoms of different matter, which leads to the ionization and destruction of these tissues, which may lead to many diseases. The concentration of radiation in the blood and urine increases; one of the most dangerous sources of radiation available is radon. **The aim is to** determine the concentration of radon gas ($^{222}Rn$) in biological samples (urine and serum) using a solid-state nuclear track detector (CR-39). **Methods**: biological samples (urine and serum) were analyzed in this study in Najaf Governorate, Iraq, of renal stone patients, renal failure patients, chronic kidney disease patients, and a group of healthy control patients in three age groups. **Results**: the mean levels of $^{222}Rn$ in urine samples for healthy controls and renal stones patients (17.27 and 22.77), the mean levels of $^{222}Rn$ in serum samples for healthy controls, renal stones patients, renal failure patients, chronic kidney disease patients (2.43, 9.83,6.99 and 4.24) respectively. **Discussion**: it was found that the $^{222}Rn$ levels are higher in urine samples compared to the serum, and the $^{222}Rn$ levels in the serum of all patients are higher than in healthy people. These differences are statistically significant $p < 0.01$, which indicates that renal stone patients and renal failure patients are associated with a significant increase in $^{222}Rn$ levels compared to healthy people. **Conclusions**: levels of $^{222}Rn$ in urine and serum can be considered as a biomarker to discriminate between patients and healthy individuals. The findings of this study can, therefore, be used as a potential diagnostic tool for kidney patients.

**Keywords**: *renal stone, renal failure, radon*

## الملخص

**الخلفية:** تؤثر المصادر الطبيعية والاصطناعية للإشعاع على الإنسان عند تعرضه لها، حيث تصدر النويدات المشعة جسيمات ألفا وبيتا، ويمكن لهذه الجسيمات أن تتفاعل مع إلكترونات الذرات المحيطة بالمادة المختلفة، مما يؤدي إلى تأين وتدمير هذه الأنسجة، مما قد يؤدي إلى العديد من الأمراض. كما تزداد تركيزات الإشعاع في الدم والبول، ومن المصادر الخطيرة للإشعاع المتاحة غاز الرادون. **الهدف:** تحديد تركيز غاز الرادون ($^{222}Rn$) في العينات البيولوجية (البول والمصل) باستخدام كاشف المسار النووي الصلب (CR-39). **الطرق:** تم تحليل العينات البيولوجية (البول والمصل) في هذه الدراسة في محافظة النجف بالعراق من مرضى حصوات الكلى ومرضى الفشل الكلوي ومرضى أمراض الكلى المزمنة ومجموعة من الأصحاء في ثلاث فئات عمرية. **النتائج:** متوسط مستويات $^{222}Rn$ في عينات البول للأشخاص الأصحاء ومرضى حصوات الكلى (17.27و 22.77)، متوسط مستويات $^{222}Rn$ في عينات المصل للأشخاص الأصحاء ومرضى حصوات الكلى ومرضى الفشل الكلوي ومرضى أمراض الكلى المزمنة (6.99,9.83,2.43 و 4.24) على التوالي.**المناقشة:** وجد أن مستويات $^{222}Rn$ أعلى في عينات البول مقارنة بالمصل، وأن مستويات $^{222}Rn$ في المصل لجميع المرضى أعلى من الأشخاص الأصحاء. هذه الاختلافات ذات دلالة إحصائية $p < 0.01$، مما يشير إلى أن مرضى حصوات الكلى ومرضى الفشل الكلوي مرتبطون بزيادة كبيرة في مستويات $^{222}Rn$ مقارنة بالأشخاص الأصحاء. **الاستنتاجات:** يمكن اعتبار مستويات $^{222}Rn$ في البول والمصل بمثابة علامة حيوية للتمييز بين المرضى والأفراد الأصحاء. وبالتالي يمكن استخدام نتائج هذه الدراسة كأداة تشخيصية محتملة لمرضى الكلى.

**الكلمات المفتاحية:** حصى الكلى، فشل كلوي، الرادون

## 1. INTRODUCTION

Natural and artificial radiation sources affect humans upon exposure, with natural sources including internal terrestrial radiation and artificial sources originating from human activities (Jha *et al*., 2024). Radionuclides emit alpha and beta particles in both cases mentioned above, and these particles can interact with the electrons of the surrounding atoms of different matter (e.g., human tissues), which leads to the ionization and destruction of these tissues, which may lead to many diseases (Demir, 2022, Arif *et al*., 2024).

In this regard, radionuclides can enter the human body through different paths from different sources such as food, vegetables, and plants (i.e., meat, fish) or through inhaling air, water, soil, and cigarettes (Bignall & Caldwell, 2021; Aswood *et al*., 2020). The concentration of radiation in the blood and urine increases when humans are exposed externally through contact with soil. (Mohan & Chopra, 2022).

One of the most dangerous sources of radiation available is radon. Radon is a colorless, odorless gas that is naturally occurring and has radioactive properties that make it toxic. It has three isotopes: $^{222}Rn$, $^{219}Rn$, and $^{220}Rn$, which originate from the decay of $^{238}U$, $^{235}U$, and $^{232}Th$, respectively. (A A Alkufi *et al*., 2024). $^{222}Rn$ is classified as the most dominant, with a radon half-life of 3.82 days, which is the longest half-life compared to the other isotopes. (Manawi *et al*., 2024, Aswood *et al*., 2020).

Radon is a carcinogenic and radioactive substance that is found naturally in the environment. About 50% of natural exposure to radiation is due to radon. Radon gas is transferred when inhaled from the lungs and then into the bloodstream (Appleton, 2012; Abbas *et al*., 2023).

Radon has been classified as a carcinogen by the International Agency for Research on Cancer (IARC), so the concentration of this gas inside the body must be determined and its risks and radioactive effects evaluated. (McColl *et al*., 2015).

One of the most important samples used as a biomarker is urine samples, which are used to evaluate the presence of toxic and radioactive pollutants inside the body. It is one of the ways to determine the level of internal exposure to radiation such as radon. (Hall *et al.*, 2017, Alves *et al.*, 2014).

Radon removal from the body occurs rapidly after inhalation and ingestion, as radon that is consumed is eliminated from the body through the breathing process (Abed *et al.*, 2024). However, the process of absorption of radon in the human body occurs through its dissolution in the blood within the digestive system and other bodily tissues. Among the noble gases, radon has the greatest solubility in fatty tissue compared to blood, making fatty tissue the primary site for radon accumulation within the body (Abass & Sharba, 2020; Papenfuß *et al.*, 2022).

When inhaling radon gas, a large part of it is expelled before it decays in the body. However, part of the inhaled radon and its atoms are transferred from the lungs to the bloodstream and thus distributed to all parts of the body, including the kidney (Chaudhury *et al.*, 2023). Kidney-related diseases have also been observed in some people exposed to radon (Salih *et al.*, 2016). This is because the kidneys receive the highest dose compared to other organs in the body after radon moves from the lungs to the kidneys through blood circulation (Koul & Koul, 2019).

The body gets rid of radioactive materials through urine, excrement, saliva, exhalation, sweat, and drinking milk (Singh & Kostova, 2024).

Radon gas can be detected by organic nuclear detectors, which are characterized by their high sensitivity and accuracy, the most important of which is the CR-39 detector. (Guo *et al.*, 2020). The CR-39 detector is used to detect and measure charged particles, such as alpha particles in biological samples, and is a plastic detector. (El Ghazaly & Hassan, 2018).

This study aimed to determine the concentration of $^{222}$Rn in biological samples (urine and serum) taken from renal stone patients who underwent lithotripsy treatment and end-stage renal failure patients who are receiving hemodialysis treatment, patients with chronic kidney disease in the early three stages of renal failure (CKD) and a group of healthy individuals in the age groups 21-30, 31-40, ≥ 41 for males and females using a solid-state nuclear track detector (CR-39) in Najaf Governorate, Iraq and to evaluate the risk of exposure to radon gas (Asker *et al.*, 2021, Othman, 2024).

## 2. MATERIALS AND METHODS

### 2.1. Materials

This study was conducted with 120 serum and urine samples from 20 patients with renal stones (serum and urine), 20 patients with end-stage renal failure (serum),20 patients with chronic kidney disease patients in the first three stages of (CKD) (serum), and 20 healthy controls (serum and urine). Twenty subjects were selected as a control group in different age groups in Najaf province, Iraq. Table (1) shows the age groups and number of samples for patients and health groups in the current study. All participants consented to be sampled. Information about age, disease type, and gender were collected. Serum and urine samples were taken from the renal stone patients' group and the healthy group. Mostly because dialysis-treated patients produce very little or no urine due to renal failure, only serum samples were taken from the two groups of end-stage renal failure and the first three stages of renal failure to participate in this study. A unique code was assigned to each study participant aged 21-30, 31-40, ≥ 41. 5 ml of blood was collected and stored in gelatin tubes.

### 2.2. Methods

The samples were then left to clot for (5-10) minutes, and centrifugation was used to separate the serum. The serum was then transferred to Eppendorf tubes with a volume of 1 ml and stored in the freezer (Sharba *et al.*, 2020). As for urine samples, 10 ml were collected and placed in urine containers, and a code was written to indicate each participant. Then, the samples were stored in the refrigerator. The samples were stored for a month to reach equilibrium between $^{222}$Rn and its parent $^{226}$Ra in the uranium series. A piece of CR-39 nuclear reagent was fixed with adhesive tape to the middle of the lower side of the lid of each container of urine and serum samples and left for 120 days. After the exposure time, the CR-39 reagent was extracted and treated for 1 h with NaOH (6.25 N) in a water bath at 98 °C. The CR-39 reagents were then placed in distilled water. A light microscope counted the number of tracks. The concentration of radon $^{222}$Rn ($C_{Rn}$) in the space of the tube was determined using the following equation (Al-Khayfawee *et al.*, 2024)

$$\rho = N_t / A \quad \text{(Eq. 1)}$$

Where ρ is the track density on the detector (Track $cm^{-2}$), $N_t$ is the average of track numbers in the grid area, and A is the visible Area under the microscope.

$$C_{Rn} = \rho / (K \cdot T) \quad \text{(Eq. 2)}$$

Where $C_{Rn}$ is the Radon concentrations ($Bq/m^3$), T is the exposure time, and K is the calibration factor of the detector ((0.2917±0.0511 track $cm^{-2}$ per $Bq \cdot m^{-3}$ $day^{-1}$) (Abdulhussein A Alkufi *et al.*, 2024a).

### 2.3. Statistical analysis:

Data was analyzed using SPSS v. 28, Numerical Data from the concentration of $^{222}Rn$ in biological samples (urine and serum) from 80 participants were expressed as mean ± standard deviation (SD), an independent t-test between two groups in urine samples, and an ANOVA for comparison among groups in serum samples. Median (IQR) interquartile range for continuous variables with non-normal. Receiver operator characteristic (ROC) curve analysis was carried out to evaluate the $^{222}Rn$ cut-off value as well as to predict the renal patients as diagnostic tests or adjuvant diagnostic tests. Calculating the area under the curve (AUC) with 95% confidence intervals, with $p < 0.05$, is considered statistically significant. More stringent significance ($p < 0.001$) was applied for ROC analyses.

## 3. RESULTS AND DISCUSSION:

### 3.1. Comparison of radon concentration between patient groups and healthy controls

The resulting data of $^{222}Rn$, which were obtained from urine and serum samples of patients and healthy groups, can be seen in Table 2. The t-test was used to compare urine groups of renal stone patients and healthy group, and the ANOVA Test was used to compare serum groups of patients and healthy group. According to the results, there was a difference between the renal stone group and the healthy group for $^{222}Rn$ ($P \leq 0.018$) for urine samples, and there is a very significant difference between patient groups and the healthy group for $^{222}Rn$ for serum samples as indicated by $P \leq 0.01$.

In general, the average concentration of $^{222}Rn$ for biological samples of serum and urine of patient groups was higher than that of healthy people in Najaf province. The global average of $^{222}Rn$ gas in the air ($Bq \cdot m^{-3}$) according to world organizations has different values, like CFR 39 $Bq \cdot m^{-3}$ (CFR,2009), WHO 100$Bq \cdot m^{-3}$ (Organization, 2009), EPA 74–148 Bq $m^{-3}$ (Zdrojewicz & Strzelczyk, 2006) and according to ICRP 200 $Bq \cdot m^{-3}$ (Tirmarche *et al.*, 2010).

The main values of radon concentrations for urine and serum samples of patient and healthy groups in the current work were lower than the global average of all limits by international organizations such as the Environmental Protection Agency, the World Health Organization, the Federal Research Council and the International Commission on Radiological Protection. In general, the results of the current work indicate that the radon gas in urine samples was higher than that of serum for all groups.

For serum samples, renal failure patients and those with chronic kidney disease have lower radon levels compared to renal stone patients, and the radon concentration of patient groups for serum samples is high compared to its concentration in serum for the healthy group in which the results are statistically significant ($P \leq 0.05$). Also, from Table 2, it can be seen that the radon concentrations in biological samples in the present study (urine and serum) have a high significance with a P-value<0.01. the mean concentration of radon $^{222}Rn$ in urine samples for healthy controls and renal stones patients (17.27), (22.77), the mean concentration of radon $^{222}Rn$ in serum samples for healthy controls, renal stones patients, end-stage renal failure patients, chronic kidney disease patients in the three stages (2.43) (9.83) (6.99) (4.24) respectively as shown in Table 2, and Figure 1.

These results may reflect the role of renal health status in controlling radon concentration in the body, as inhaled radon can expose the body's organs to radiation, and the most dangerous organ to be exposed to after the lungs is the kidney in the human body. The results were statistically significant, as shown in Table 2.

### 3.2. Roc curve for radon concentration of urine samples for renal stone patients

Roc curve indicates the sensitivity and specificity of radon concentration of urine samples for renal stone patients, Cut-off point was (26.6035), AUC = (0.69), P value < 0.044, 95%CI (0.522 - 0.850). The sensitivity was (0.300), while the specificity was 1. The diagnostic test moderately differentiates between patients and healthy individuals based on urine radon concentration. The p-value is less than 0.05, which means that the results are statistically significant, i.e., there is a real difference between radon levels in patients and healthy individuals and is not due to chance, indicating a relationship between urine radon concentration as a diagnostic tool and the likelihood of having renal stones (as a result of treatment or disease) compared to healthy individuals, as in Table 3 and Figure 2.

### 3.3. Roc curve for radon concentration for all patients in serum samples

Roc curve indicates the sensitivity and specificity for radon concentration of serum samples for all patients; Cut-off point was (4.9597), AUC = (0.917), P value < 0.0001, 95%CI (0.857- 0.977). The sensitivity was (0.717) while the specificity was (1). The test has a very good discriminatory ability between patients and healthy individuals, indicating that the test is very effective in discriminating between patients and healthy individuals, with good sensitivity and perfect specificity. The p-value indicates that there is a strong statistically significant difference between the two groups (patients and healthy individuals), as can be seen in Table 4 and Figure 3.

## 4. CONCLUSION

The results obtained for radon concentrations of urine and serum samples of patients and healthy subjects in the present work were lower than the global average of all limited international organizations, such as the World Health Organization, the Federal Research Council, and the International Commission on Radiological Protection, the Environmental Protection Agency. According to the comparisons made in this study, it was found that the radon concentration is higher in urine samples compared to the serum of renal stone patients and healthy people, respectively, and the radon concentration in general in the serum of all patients is higher than healthy people. These differences are statistically significant p < 0.01, which indicates that renal stone patients and renal failure patients are associated with a significant increase in radon concentration compared to healthy people. The concentration of $^{222}Rn$ in urine and serum can be considered an excellent biomarker with a high ability to discriminate between patients and healthy individuals, supported by high AUC and strong statistical significance. The findings of this study can, therefore, be used as a potential diagnostic tool for patients with different clinical kidney cases.

## 5. DECLARATIONS

### 5.1. Study Limitations

The relatively small sample size of 120 serum and urine samples may limit the generalizability. Exclusion criteria omitted participants with certain health conditions, potentially introducing bias. The cross-sectional design prevents establishing causal relationships. Reliance on self-report measures, which may introduce measurement error. Potential confounding variables were not accounted for in the statistical analysis. Lack of control for external factors.


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### 5.4. Competing Interests

The authors declare that they do not have any potential conflict of interest in this publication.

### 5.5. Open Access



## 6. HUMAN AND ANIMAL-RELATED STUDIES

### 6.1. Ethical Approval

This cross-sectional study comprised one hundred and twenty (120) serum and urine samples for (males and females) with ages ranging from (21, ≥ 41) years, performed based on ethical clearance in line with the Declaration of Helsinki and verbally approved by the Ethics Committee of the Kufa University, with approval number of (2013) and date of (21/02/2024).

### 6.2. Informed Consent

Participants in the study provided written informed consent, and formal data were coded and recorded for each participant. This included information such as name, age, gender, and type of disease.

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***Table 1.*** *General characteristics of the studied groups*

| Categories | | healthy control | renal stone | renal failure | CKD | p-value |
|---|---|---|---|---|---|---|
| Age (year) mean ± SD | | 39.30±12.18 | 41.35±10.17 | 50.3±13.56 | 40.75±14.03 | 0.032*# |
| Age groups | 21-30 | 5(25.0%) | 4(20.0%) | 3(15.0%) | 7(35.0%) | 0.116 Ns |
| | 31-40 | 6(30.0%) | 8(40.0%) | 2(10.0%) | 5(25.0%) | |
| | ≥ 41 | 9(45.0%) | 8(40.0%) | 15(75.0%) | 8(40.0%) | |
| Sex | Male | 10(50.0%) | 10(50.0%) | 10(50.0%) | 10(50.0%) | 1.00 Ns |
| | Female | 10(50.0%) | 10(50.0%) | 10(50.0%) | 10(50.0%) | |

***Table 2.*** *Comparison of radon concentration between patient groups and healthy controls for urine and serum samples*

| Groups | | $^{222}Rn$ (Bq $m^{-3}$) | |
|---|---|---|---|
| | | serum | urine |
| healthy control | N | 20 | 20 |
| | Mean | 2.43 *D | 17.27 *B |
| | SEM | 0.33 | 1.34 |
| | SD | 1.47 | 5.98 |
| | Min-Max | 0.90-4.51 | 8.12-25.25 |
| | Median (IQR) | 1.80(0.90-3.60) | 17.14(11.27-23.45) |
| renal stone | N | 20 | 20 |
| | Mean | 9.83 *A | 22.77 *A |
| | SEM | 0.72 | 1.77 |
| | SD | 3.23 | 7.92 |
| | Min-Max | 6.31-18.04 | 13.53-36.98 |
| | Median (IQR) | 9.02(7.21-11.50) | 21.19(15.56-29.31) |
| renal failure | N | 20 | |
| | Mean | 6.99 *B | |
| | SEM | 0.43 | |
| | SD | 1.92 | |
| | Min-Max | 4.51-9.92 | |
| | Median (IQR) | 6.31(5.41-9.02) | |
| CKD | N | 20 | |
| | Mean | 4.24 *C | |
| | SEM | 0.37 | |
| | SD | 1.66 | |
| | Min-Max | 2.71-7.21 | |
| | Median (IQR) | 3.60(2.71-5.41) | |
| | p-value | F=44.16<br><0.001 | T= -2.48<br>0.018* |

***Table 3.*** *Roc curve data for radon concentration for renal stone patients in urine samples*

| Area Under the ROC Curve renal stone / healthy control in urine | | | | | | | |
|---|---|---|---|---|---|---|---|
| Samples Type | Predicts | Area (AUC) | p-value | 95%CI | Cut-off Point | Se. | Sp. |
| urine | $^{222}Rn$ (Bq $m^{-3}$) | 0.69 | P< 0.044* | 0.522 - 0.850 | 26.6035 | 0.300 | 1 |

***Table 4.*** *Roc curve for radon concentration for All patients in serum samples*

| Area under the ROC Curve All patients / healthy control in serum | | | | | | | |
|---|---|---|---|---|---|---|---|
| Samples Type | Predicts | Area (AUC) | p-value | 95%CI | Cut-off Point | Se. | Sp. |
| serum | $^{222}Rn$ (Bq $m^{-3}$) | 0.917 | P< 0.0001** | 0.857- 0.977 | 4.9597 | 0.717 | 1 |

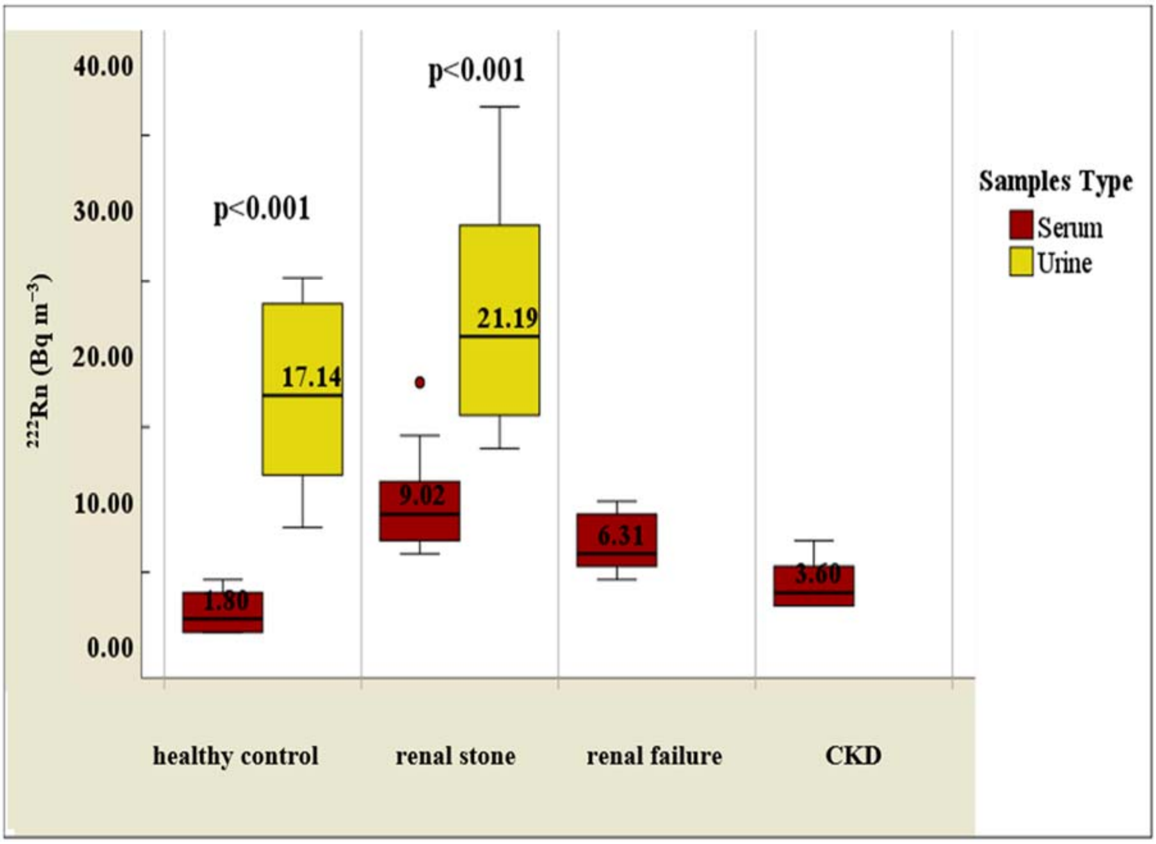


***Figure 1.*** *A comparison of radon concentration median (IQR) among patient groups and healthy controls for urine and serum*

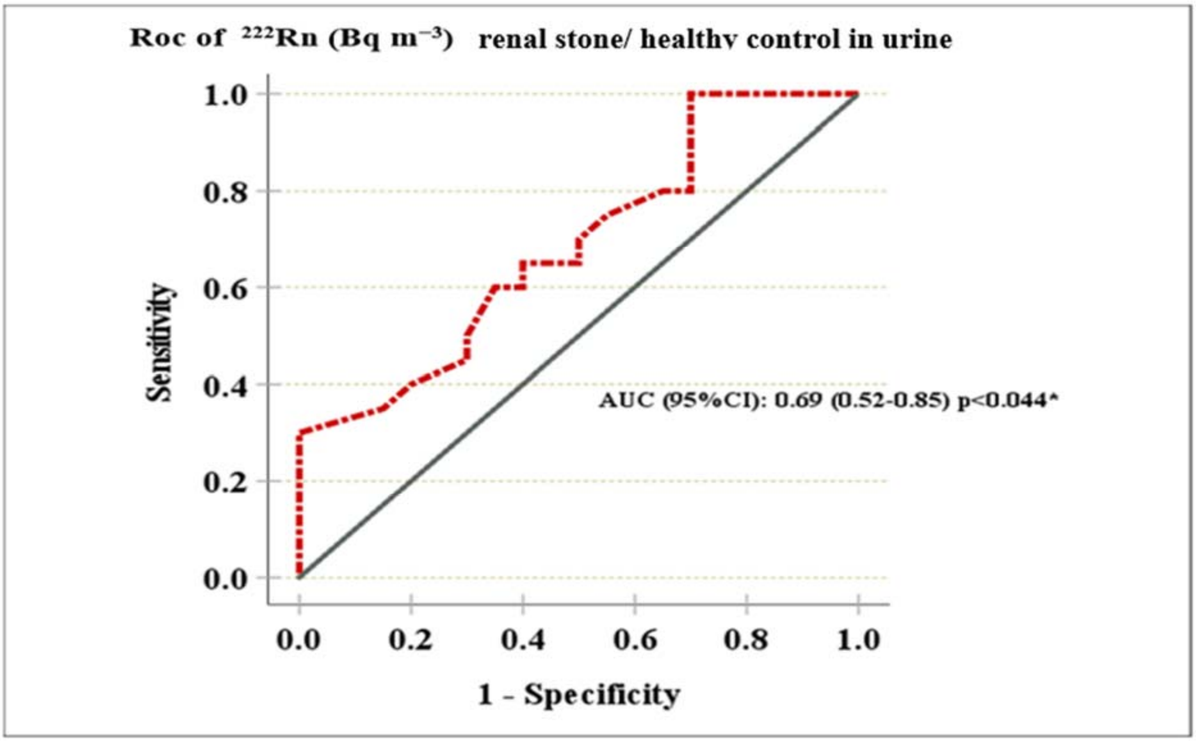


***Figure 2.*** *Roc curve of renal stone patients with healthy control in urine samples*

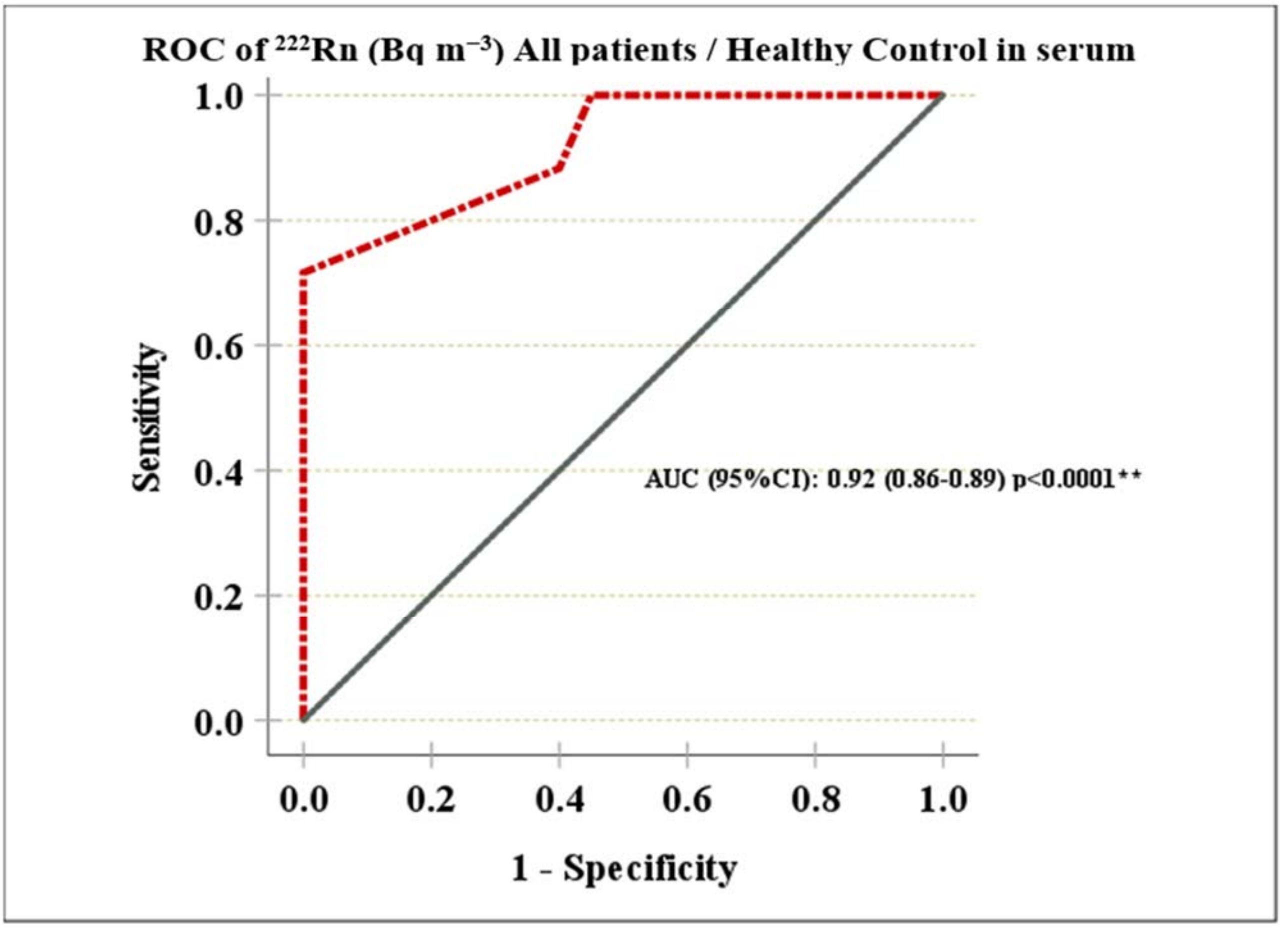


***Figure 3.*** *Roc curve of all patients and healthy control in serum samples*