DOI: 10.7860/JCDR/2023/61635.17475

Original Article

Internal Medicine Section

Spectrum of Renal Involvement in Cancer Patients: A Cross-sectional Descriptive Study

PIDENO NGULLIE[1], SMITA NATH[2], ALPANA RAIZADA[3], SUNIL AGARWAL[4]

ABSTRACT

Introduction: Cancer is associated with multiple renal manifestations like Acute Kidney Injury (AKI), Chronic Kidney Disease (CKD), proteinuria, and electrolyte imbalance. The reason behind renal dysfunction in cancer patients is multifactorial and can be attributed to underlying cancer and treatment modalities, in addition to co-morbidities surgical procedures and infections.

Aim: To assess the spectrum of renal involvement in cancer patients presenting at a tertiary care hospital.

Materials and Methods: The cross-sectional descriptive study, was conducted in the Department of Medicine of University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India. One hundred consecutive patients referred for nephrology consultation with diagnosed cancer, irrespective of cancer aetiology between the age group of 15-70 years with deranged kidney function test were recruited. Detailed medical and treatment history, including the type of cancer-solid or haematological, cancer status-cured or continuing, treatment given-chemotherapy, radiotherapy or surgery or a combination and associated co-morbidities like diabetes mellitus and hypertension were recorded. Routine investigations and special investigations, including assessment of estimated Glomerular Filtration Rate (eGFR) and estimation of Albumin-Creatinine Ration (ACR) was done. Patients were then segregated, based on their kidney function test into groups with AKI or CKD and underlying cause was valuated. Summary statistics was presented as mean, median or frequency and data analysed using Statistical Package of Social Sciences (SPSS) version 24.0.

Results: The mean age of the study population was 53.73±12.20 years with 63% male and 37% female participants; 87% patients had solid cancers, while 13% had haematological cancers. The median duration, since the diagnosis was seven months and the patients were undergoing chemotherapy, radiotherapy or a combination of both; seven patients had surgery for underlying malignancy and an additional six had received chemotherapy or radiation therapy along with surgery. At the time of recruitment, 78% patients had AKI and 22% patients were diagnosed with CKD. Chemotherapy-induced nephropathy was the most common cause of AKI (n=46). In the CKD group diabetes (n=7) was the most common aetiology.

Conclusion: The kidneys in cancer patients can be involved in a number of ways, as a consequence of the cancer itself, its treatment, superimposed infections or associated co-morbidities. Chemotherapy-induced nephropathy is the most common cause of AKI, whereas, diabetes is the most common cause of CKD in cancer patients.

Keywords: Acute kidney injury, Chronic kidney disease, Malignancy

INTRODUCTION

Among non communicable diseases, cancer is one of the leading causes of morbidity globally [1]. Kidney involvement invariably complicates the course of underlying cancer and increases risk of renal dysfunction as a consequence of the cancer itself (myeloma kidney, urinary tract obstruction), its treatment (acute tumour lysis syndrome, drug-induced nephropathy, major surgical procedures), associated complications (sepsis, hypercalcaemia) and co-morbidities [2,3]. Kidney involvement can occur in form of AKI or CKD, proteinuria and electrolyte imbalance. Literature suggests that risk of AKI can be attributed to detriments like metastasis to kidneys, use of nephrotoxic drugs and radiations. The overall prevalence of AKI in cancer is comparable to other critical conditions like patients admitted to Intensive Care Unit (ICU), where AKI can be present in 20-50% patients [4-6].

The prevalence of cancer-related AKI is reported between 20%-30% [7]. Similar studies carried out in Danish population, estimated the prevalence of AKI 30-40% [8]. Similarly, cancer and CKD are closely related as CKD can be a complication, as well as, predisposing factor for cancer [9]. Co-morbidities like diabetes, cardiovascular insufficiency, hypertension not only increase the predisposition to AKI, but also contribute to burden of CKD in cancer patients. Besides AKI, CKD is also a complication, which occurs during course of malignancy and it's treatment [9,10].

Observational studies involving more than 4000 cancer patients have reported prevalence of stage 3 CKD of upto 30%. In these studies stage 4 CKD was present in between 1% and 8.3% patients. A Korean cohort study involving more than 8,00,000 cancer patients matched for age, sex, eGFR, and co-morbidities with a control group 16,48,730 patients revealed that cancer patients with CKD had higher requirement of renal replacement therapy and increased risk of death [10]. The relationship between CKD and cancer is reciprocal as CKD increase predisposition for development of a number of malignancies [11].

Kidney disease is one the most common complications associated with haematological malignancies like lymphomas and leukaemia in addition to paraproteinaemia and multiple myeloma [12]. Almost 50% patients with multiple myeloma develop either AKI or CKD during course of their illness. Among paraproteinaemia single centre retrospective study found that amyloidosis, monoclonal IgM cryoglobulinemia, lymphoplasmacytic lymphoma infiltration light chain deposition disease and light chain cast nephropathy were associated with renal dysfunction. In Chronic Lymphocytic Leukaemia (CLL) patient's membranous glomerulonephritis was the most common kidney pathology found on biopsy. A 40% of kidney biopsy revealed infiltration of CLL in kidneys. Among solid cancers urogenital malignancies are the underlying malignancy in upto 46% patients [13,14].

The development of renal impairment in turn, further hampers the treatment prospects in this group of patients by imposing limitations in the institution of full dosage of certain anticancer drugs for fear of toxicity, due to its reduced clearance [5]. Renal dysfunction is associated with adverse short and long-term outcomes with some studies concluding the 60-day survival at 14%. Hence, renal dysfunction in cancer patients leads to an additional cause of morbidity and mortality in already predisposed individuals. Additionally, patients require frequent assessment of renal functions in order to monitor on going therapies for evidence of nephrotoxicity as proper dosing of chemotherapeutic agents. Cancer and its treatment in patients with renal dysfunction add to cost of healthcare, in addition to longer hospital stay and increased mortality [15].

The focus of most of these studies is either AKI or CKD. Review of literature revealed very few studies focusing on both these aspects of renal function. Therefore, for the present study authors choose to incorporate cancer patients with AKI as well as CKD. The incidence of kidney dysfunction reveals wide variation among different study population and limited literature is available from India. The authors, also observed that most of studies focus on single type of cancer. The aim of present study was assess different causes of renal failure in cancer patients. A study like this becomes important, where, the authors can study the diverse spectrum and cause of renal involvement in cancer patients in Indian setting.

MATERIALS AND METHODS

The cross-sectional descriptive study was conducted in Department of Medicine of University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India. The study was undertaken after approval from Institutional Ethical Committee vide letter no. IECHR-51-9-R1. Using convenience sampling method one hundred consecutive diagnosed cases of any type of cancer with deranged kidney function test referred for nephrology consultation were recruited. The patients recruited were between age of 15-70 years.

Inclusion criteria: All consenting patients between ages of 15 and 70 years with deranged renal function, were included in the study.

Exclusion criteria: Patients who did not give their consent for participation, were excluded.

Study Procedure

Detailed medical and treatment history, including the type of cancer-solid or haematological, cancer status-cured or continuing, treatment given-chemotherapy, radiotherapy or surgery or a combination and associated co-morbidities like diabetes mellitus and hypertension were recorded. General physical and systemic examination was done. Routine investigations and special investigations including assessment of eGFR and estimation of ACR were done. AKI and CKD were diagnosed on basis of KDOQI Guidelines of National Kidney foundation, USA [16,17,18].

STATISTICAL ANALYSIS

Summary statistics was presented as mean, median or frequency as deemed appropriate. Unpaired t-test will be used to compare mean values. The data was entered into a computer based spread-sheet and analysed using (SPSS) version 24.0.

RESULTS

The mean age of all the study subjects was 53.73±12.20 years and the study population consisted of 63% male participants and 37% female participants. The baseline laboratory parameters are given in [Table/Fig-1].

Overall, 87% patients had solid cancers and 13% had haematological cancers. Of the solid cancers, the most common diagnosis was carcinoma cervix which was present in 25.28% (n=22) followed by carcinoma oropharynx at 19.54% (n=17) [Table/Fig-2]. In haematological cancer category, lymphoma was the most common type (46%), followed by multiple myeloma at 30% [Table/Fig-2].

Laboratory parameters	AKI (n=78) Mean±SD	CKD (n=22) Mean±SD
Haemoglobin (mg/dL)	9.74±2.30	9.28±1.84
Blood urea (mg/dL)	98.05±52.80	94.50±61.14
Serum sodium (mEq/L)	138.35±6.20	138.81±5.06
Serum potassium (mEq/L)	4.69±0.88	4.79+0.92
Total protein (mg/dL)	6.80±1.10	6.67±1.27
Serum albumin (mg/dL)	3.40±0.81	3.37±1.00
Serum calcium (mg/dL)	8.46±1.46	8.25±2.27
Serum uric acid (mg/dL)	6.58±2.02	5.65±1.69

[Table/Fig-1]: Baseline laboratory parameters of study population.

Type of cancer	Number
Carcinoma cervix	22
Carcinoma oropharynx	17
Lymphoma	6
Multiple myeloma	4
Carcinoma oesophagus	6
Carcinoma urinary bladder	6
Carcinoma lung	6
Carcinoma prostate	5
Carcinoma rectum	3
Carcinoma breast	3
Carcinoma ovary	3
Carcinoma larynx	3
Carcinoma pancreas	2
Renal cell carcinoma	2
Acute lymphocytic leukaemia	2
Chronic myeloid leukaemia	1
Malignant melanoma	1
Hepatocellular carcinoma	1
Endometrial carcinoma	1
Carcinoma small intestine	1
Carcinoma ascending colon	1
Carcinoma testis	1
Carcinoma gall bladder	1
Unknown primary with metastasis	1

[Table/Fig-2]: Type of cancer.

Hypertension was the most common co-morbidity followed by combination of diabetes and hypertension, which were found in six patients [Table/Fig-3].

Co-morbidities	Number
Hypertension	19
Diabetes	5
Diabetes and hypertension	6
CAD	3
Hypothyroidism	3
Pulmonary tuberculosis	1
HIV	1
COPD	1
CVA	1
Total	40

[Table/Fig-3]: Co-morbidities in study population.
CAD: Coronary artery disease; HIV: Human immunodeficiency virus; COPD: Chronic obstructive pulmonary disease; CVA: Cerebrovascular accident

At the time of recruitment out of the 100 participants, 78% had renal involvement due to AKI and 22% patients had renal involvement due to CKD. In the 78 patients, who had AKI, 8 (10.2%) had a prerenal cause, 48 (61%) had a renal cause and 22 (28%) had a postrenal cause [Table/Fig-4].

Cause of AKI	Type of AKI	No. of cases (n=78)
Sepsis	Prerenal AKI	8
Chemotherapy induced AKI	Renal	46
Multiple myeloma	Renal	2
Obstructive uropathy	Postrenal	21
Tumour lysis syndrome	Postrenal	1

[Table/Fig-4]: Causes of AKI.

All of the eight patients with prerenal, AKI had solid cancers and AKI was attributed to sepsis, in all of them. In the 48 patients with renal cause for AKI, 46 (95%) patients had chemotherapy induced nephrotoxicity, while 2 (5%) cases had multiple myeloma, associated renal dysfunction. In the 46 patients with chemotherapy induced nephrotoxicity, the most common cancer seen was carcinoma oropharynx (n=12) and the most common drug used in these 46 patients was cisplatin (n=32).

In the present study, 22 (28%) patients with postrenal AKI, 21 (95%) had obstructive uropathy. The most common form of cancer in these patients was carcinoma cervix (n=11). One of the patients had tumour lysis syndrome [Table/Fig-5].

Type of cancer	No. of cases (n)
Carcinoma cervix	11
Carcinoma prostate	4
Carcinoma urinary bladder	2
Lymphoma	2
Carcinoma ovary	1
Carcinoma endometrium	1

[Table/Fig-5]: Cancers causing extra renal obstruction.

In the 22 patients with CKD, 7 (32%) had diabetes, 6 (28%) had hypertension. Six (28%) had stopped treatment for cancers of the urogenital system which led to development of obstructive uropathy and subsequently CKD. Carcinoma ovary was the most common cause of obstructive uropathy associated CKD (n=3), followed by carcinoma ovary (n=2) and carcinoma urinary bladder (n=1). Two (9%) had multiple myeloma and one was an operated case of renal cell carcinoma, with solitary kidney.

In the present study, the median serum creatinine was 2.3 mg/dL, for the entire study population. Microscopic urine analysis revealed presence of pus cells in 27 patients, out of which 21 patients were from the AKI group. Albumin Creatinine Ratio (ACR) revealed presence of microalbuminuria in 82% participants. Sixty seven patients with AKI had either micro or macroalbuminuria. All 22 of CKD patients, had micro or macroalbuminuria. Ultrasonography revealed normal kidney morphology in 50% participants. Bilateral hydroureteronephrosis was the most common structural anomaly detected on ultrasonography and was present in 27% patients.

The mean eGFR in patients with AKI was 26.88±14.42 mL/min/1.73 m^2. In patients with CKD the mean eGFR was 24.09±13.94 mL/min/1.73 m^2. Based on eGFR stage 3 CKD was present in nine patients. Eight patients had stage 5 CKD and remaining five had stage 4 CKD.

DISCUSSION

The association between cancer and kidney disease has long been recognised but received better attention after the creation of a 'new' nephrological subspeciality called 'Onconephrology' [19]. Renal dysfunction often complicates the clinical course and management of cancer. The ambit of renal dysfunction in cancer, include both AKI, as well as, CKD. The renal dysfunction can be secondary to either patient or disease specific factors in addition to drug induced nephrotoxicity [10,20]. In the present study, of all the patients who presented with kidney dysfunction, larger proportion had AKI (78%) as compared to CKD (22%). The most common cancers was carcinoma cervix, which was found in 22% patients followed carcinoma oropharynx at 17% and carcinoma bladder lymphoma, carcinoma oesophagus, and carcinoma lungs at 6% each. In a Danish population based cohort study, which is a large study on incidence of AKI in cancer patients, 9631 cancer patients had AKI out of a total of 37,267 incident cancer patients. The commonest cancer reported were, that of lungs cancer (n=1225), colon cancer (n=1104), prostate cancer (n=915) and urinary bladder (n=791) [8]. A similar study carried out in 44 academic and local hospitals in China, reported that gastrointestinal malignancy followed by genitourinary malignancy, as the most common form of cancer associated with renal dysfunction. Present study, however, was not comparable with the above study, probably because of a smaller sample size.

In the present study, causes of AKI patients were segregated into prerenal, renal and postrenal causes. In the prerenal group, there were 11% (n=8) patients. Sepsis was the cause of AKI, out of which only one survived. In a landmark study by Heeg M et al., they found that sepsis with AKI in cancer patients was associated with mortality rates of 100% in non solid cancers [19].

Largest proportion of the patient with AKI had intrinsic renal aetiology of AKI (61%). It was observed that most common cause was chemotherapy. It was present in 95% patients in this group followed by multiple myeloma (5%) associated kidney involvement. Multiple myeloma was associated with both AKI and CKD. In the present study, there were two cases of multiple myeloma-associated AKI in addition to two multiple myeloma patients with history of CKD. It was difficult to isolate the responsible drug because most of them had received combination therapy, however the maximum incidence was observed in patients receiving cisplatin based chemotherapy (95%). Forty six of the patients received chemotherapy, out of which, 32 (69.56%) had been treated with cisplatin-based therapy. A study by Kitchlu A et al., revealed that the overall rate of AKI in patients receiving chemotherapy was 5.9% and the risk of AKI significantly increased after 90 days of chemotherapy [20]. In another study by Bagri PK et al., cisplatin induced nephropathy in head and neck cancer was compared with carcinoma cervix with obstructive uropathy during concurrent chemoradiation, and it was found to be higher in head and neck cancer. The reason being, that with concurrent chemoradiation, as the 3rd-4th week is reached, oral mucosal reactions increase and affect oral intake ($p<0.001$) which further adds to cisplatin induced nephrotoxicity, whereas in carcinoma cervix oral intake of water is not impaired [21].

In the postrenal group of AKI, almost all the patients had extra renal obstruction (95%) due to either cancer of the urogenital system or retroperitoneal lymphadenopathy and only one was due to tumour lysis syndrome. Carcinoma cervix (n=11) was found to be the most common cause of extra renal obstruction. In a study by Olivera AT et al., on 42 patients with obstructive nephropathy due to malignancies, it was observed that the highest number of cases was observed with carcinoma cervix (n=12) followed by bladder tumour (n=9) [22].

In the present study, 22% of the patients had CKD at the time of recruitment. Out of this, maximum was seen to be associated with diabetes in 32% patients (n=7) followed by hypertension and cancers of the urogenital system in 28% patients (n=6). All the patients of urogenital cancer had defaulted treatment. The laboratory investigation revealed that Urinary Tract Infection (UTI), was the most common infection, which was present in 27% study population. A total of 77% of UTI patients were in group with AKI. Microalbuminuria was detected in 82% patients. Notably, 100% CKD patients had microalbuminuria.

Radiological investigations revealed bilateral hydroureteronephrosis as the most common structural anomaly. Based on eGFR, most patients with CKD were in stage 3. Similar studies have demonstrated eGFR <90 mL/min/1.73 m^2 in upto 50% patients [19]. Age, type of neoplasm and co-morbidities like hypertension and diabetes have an impact of prevalence and severity of CKD [11,19,22].

Among non communicable diseases, cancer has emerged as one of the leading cause of morbidity and mortality. AKI alone or superimposed on CKD, have been found in wide variety of neoplasm as demonstrated, in the present study and can have far reaching impact on treatment and outcome of cancer. To the best of authors' knowledge limited data related to renal dysfunction is available from Indian cohort. Therefore, authors hope to increase awareness regarding renal dysfunction in cancer among clinicians.

Limitation(s)

However, the present study comes with certain limitations with the most important one, being the small sample size and the cross-sectional nature of the study, which made it difficult to make a projection representative of the actual scenario and its prognostic outcomes. Another limitation is that, only cancer patients with deranged kidney function were studied, therefore, the incidence and the risk of AKI in relation to the type of cancer could not be evaluated. In conclusion, perhaps a study with a prospectively followed cohort, substantially large sample size and longer time span, will yield a better result and help clinicians involved in the treatment, to achieve a better understanding of the complexity involved in the management of these group of patients, so as to improve their quality of life.

CONCLUSION(S)

The kidneys in cancer patients can be involved in a number of ways, as a consequence of the cancer itself, its treatment, superimposed infections or associated co-morbidities, leading to an additional risk of morbidity and mortality. However, the increased proportion of chemotherapy induced nephropathy leading to AKI, calls for interventions, to reduce kidney injury, due to treatment.

REFERENCES

[1] Wang H, Naghavi M, Allen C, Barber RM, Carter A, Casey DC, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: A systematic analysis for the global burden of disease study 2015. Lancet. 2016;388(10053):1459-544.

[2] Nazzal Z, Abdeljaleel F, Ashayer A, Salameh H, Hamdan Z. The rate and risk factors of acute kidney injury among cancer patients' admissions in Palestine: A single-center study. Int J Nephrol. 2022;2022:2972275.

[3] Chinnadurai R, Flanagan E, Jayson GC, Kalra PA. Cancer patterns and association with mortality and renal outcomes in non dialysis dependent chronic kidney disease: A matched cohort study. BMC Nephrol. 2019;20:380. https://doi.org/10.1186/s12882-019-1578-5.

[4] Cheng Y, Nie S, Li L, Li Y, Liu D, Xiong M, et al. Epidemiology and outcomes of acute kidney injury in hospitalised cancer patients in China. Int J Cancer. 2019;144(11):2644-50.

[5] Péron J, Neven A, Collette L, Launay-Vacher V, Sprangers B, Marreaud S. Impact of acute kidney injury on anticancer treatment dosage and long-term outcomes: A pooled analysis of European Organisation for Research and Treatment of Cancer trials. Nephrol Dial Transplant. 2020:gfaa049.

[6] Melo AF, Macedo FD, Bezerra EF, Lopes de Melo AC, Mehta WA, Almeida RL, et al. A systematic review and meta-analysis of acute kidney injury in the intensive care units of developed and developing countries. Plos One. 2020;15(1):e0226325. https://doi.org/10.1371/journal.pone.0226325.

[7] Jin J, Wang Y, Shen Q, Gong J, Zhao L, He Q. Acute kidney injury in cancer patients: A nationwide survey in China. Sci Rep. 2019;9(1):3540.

[8] Christiansen CF, Johansen MB, Langeberg WJ, Fryzek JP, Sørensen HT. Incidence of acute kidney injury in cancer patients: A Danish population-based cohort study. Eur J Intern Med. 2011;22(4):399-406.

[9] Iff S, Craig JC, Turner R, Chapman JR, Wang JJ, Mitchell P, et al. Reduced estimated GFR and cancer mortality. Am J Kidney Dis. 2014;63:23-30.

[10] Kim CS, Kim B, Suh SH, Oh TR, Kim M, Choi HS, et al. Risk of kidney failure in patients with cancer: A south Korean population-based cohort study. Am J Kidney Dis. 2022;79(4):507-517.e1.

[11] Ciorcan M, Chisavu L, Mihaescu A, Gadalean F, Bob FR, Negru S, et al. Chronic kidney disease in cancer patients, the analysis of a large oncology database from Eastern Europe. PLoS ONE. 2022;17(6):e0265930. https://doi.org/10.1371/journal.pone.026593.

[12] Chauvet S, Bridoux F, Ecotière L, Javaugue V, Sirac C, Arnulf B, et al. Kidney diseases associated with monoclonal immunoglobulin M-secreting B-cell lymphoproliferative disorders: A case series of 35 patients. Am J Kidney Dis. 2015;66:756-67.

[13] Higgins L, Nasr SH, Said SM, Kapoor P, Dingli D, King RL, et al. Kidney involvement of patients with Waldenström Macroglobulinemia and other IgM-producing B Cell lymphoproliferative disorders. Clin J Am Soc Nephrol. 2018;13:1037-46.

[14] Strati P, Nasr SH, Leung N, Hanson CA, Chaffee KG, Schwager SM, et al. Renal complications in chronic lymphocytic leukemia and monoclonal B-cell lymphocytosis: the Mayo Clinic experience. Haematologica. 2015;100:1180-88.

[15] Park SE, Hwang JH, Choi JH, Kim SH, Choi JC, Jang JS, et al. Incidence, risk factors, and clinical outcomes of acute kidney injury caused by palliative chemotherapy in lung cancer. J Cancer. 2019;10(22):5332-38. https://www.jcancer.org/v10p5332.htm.

[16] Summary of recommendation statement. Kidney Int Suppl. 2012;2(1):08-12.

[17] KDOQI Clinical practice guidelines for bone metabolism and diseases in chronic kidney disease. http://www.kidney.org/profesionals/kdoqi/guidelines_bone/refrence.htm. Accessed on 10th April 2022.

[18] Cosmai L, Porta C, Gallieni M, Perazella MA. Onco-nephrology: A decalogue. Nephrol Dial Transplant. 2016;31(4):515-19.

[19] Heeg M, Mertens A, Ellenberger D, Muller GA, Patschan D. Prognosis of AKI in malignant diseases with and without sepsis. BMC Anesthesiol. 2013;13(1):36.

[20] Kitchlu A, McArthur E, Amir E, Booth CM, Sutradhar R, Majeed H, et al. Acute kidney injury in patients receiving systemic treatment for cancer: A population-based cohort study. J Natl Cancer Inst. 2019;111(7):727-36.

[21] Bagri PK, Kapoor A, Kalwar A, Singhal MK, Singh D, Narayan S. Comparative analysis of Cisplatin-induced nephrotoxicity in head and neck cancer and carcinoma cervix during concurrent chemoradiotherapy. South Asian J Cancer. 2014;3(4):217-20.

[22] Olivera AT, Gjulsen S, Katica Z. Obstructive nephropathy as a result of malignant neoplasms: A single centre experience. BANTAO Journal. 2010;8(2):71-74.

PARTICULARS OF CONTRIBUTORS:

1. Consultant, Department of Medicine, Eden Medical Centre, Dimapur, Nagaland, India.
2. Assistant Professor, Department of Medicine, University College of Medical Sciences, New Delhi, India.
3. Professor, Department of Medicine, University College of Medical Sciences, New Delhi, India.
4. Ex-Professor, Department of Medicine, University College of Medical Sciences, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Alpana Raizada,
Professor, Department of Medicine, University College of Medical Sciences,
New Delhi-110095, India.
E-mail: alpanaraizadakharya@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Nov 19, 2022
- Manual Googling: Dec 17, 2022
- iThenticate Software: Dec 30, 2022 (9%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Nov 18, 2022**
Date of Peer Review: **Dec 10, 2022**
Date of Acceptance: **Jan 02, 2023**
Date of Publishing: **Feb 01, 2023**