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EXPLORING URIC ACID PROFILE IN DIABETIC NEPHROPATHY: A CROSS-SECTIONAL INVESTIGATION

Original Research

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ABSTRACT

Background: Diabetes mellitus, particularly type 2, is a growing global health concern, with diabetic nephropathy being a leading microvascular complication. Serum uric acid (SUA), while physiologically an antioxidant, has been increasingly implicated in oxidative stress and renal impairment when chronically elevated. Hyperuricemia may contribute to the progression of diabetic kidney disease, making its early detection vital in managing long-term renal outcomes.

Objective: To determine the frequency of hyperuricemia in type 2 diabetic patients with nephropathy and to evaluate its relationship with diabetic kidney dysfunction in a local population.

Methods: This descriptive cross-sectional study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar, from 1st September 2024 to 28th February 2025. A total of 139 patients, aged 30 to 70 years, with confirmed diabetic nephropathy were included using convenience sampling. Diabetic nephropathy was identified by a urinary albumin-to-creatinine ratio (UACR) >30 mg/g, and diabetes was confirmed by HbA1c >6.5% or a history of antidiabetic therapy exceeding six months. Hyperuricemia was defined as SUA >6.0 mg/dL. Fasting blood samples were analyzed using Selectra XL chemistry analyzer. Data were processed using SPSS v20. Quantitative data were expressed as mean ± SD, and categorical variables were analyzed using Chi-square or Fisher's exact test.

Results: The mean age of participants was 50.20 ± 6.17 years, with a mean BMI of 24.38 ± 2.71 kg/m² and a mean SUA level of 6.09 ± 1.74 mg/dL. Among the 139 patients, 119 (85.6%) were older than 45 years and 80 (57.6%) were male. Hyperuricemia was observed in 36 individuals (26.0%). A significant positive correlation was noted between SUA and both UACR ($r = 0.949$, $p < 0.001$) and diabetes duration ($r = 0.955$, $p < 0.001$).

Conclusion: Elevated serum uric acid levels were prevalent among diabetic patients with nephropathy and significantly associated with worsening albuminuria and longer disease duration. Routine monitoring of uric acid in diabetic care may help identify individuals at risk for renal complications and guide early intervention strategies.

Keywords: Diabetes Mellitus, Diabetic Nephropathy, Hyperuricemia, Kidney Diseases, Oxidative Stress, Serum Uric Acid, Type 2 Diabetes Mellitus.

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INTRODUCTION

Diabetes mellitus (DM) has emerged as a rapidly escalating public health issue over the past few decades, with type 2 diabetes mellitus (T2DM) accounting for more than 90% of all diagnosed cases. The World Health Organization reported that by the end of the second decade of the 21st century, over 420 million individuals globally were living with diabetes, and this number is projected to surpass 500 million by the year 2040 (1). Not only is diabetes a major cause of morbidity and mortality worldwide, but it also ranks as the third leading contributor to disability and death globally (2). In many low- and middle-income countries, including Pakistan, the prevalence of diabetes is increasing at an alarming rate, with recent estimates suggesting that over 13.7% of the population is either diagnosed with or at risk of developing diabetes mellitus (3). Among the multitude of complications associated with diabetes, both microvascular and macrovascular complications have a profound impact on patients' quality of life. Diabetic nephropathy, a major microvascular complication, stands out as a leading cause of end-stage renal disease (ESRD). It has been observed that approximately 12% of individuals newly diagnosed with T2DM already exhibit signs of diabetic nephropathy (4). This underscores the necessity of early identification and risk stratification to prevent irreversible renal damage. Uric acid, the final product of purine metabolism in humans, is generated through the enzymatic action of xanthine oxidoreductase, which oxidizes xanthine. Unlike many other mammals, humans lack the enzyme uricase, resulting in comparatively higher serum uric acid (SUA) levels (5). The pathophysiological role of uric acid in human disease has garnered increasing attention, especially due to its dual role as both an antioxidant and a pro-inflammatory agent depending on its biochemical environment. Elevated SUA levels have been implicated in a range of metabolic and cardiovascular conditions including insulin resistance, central obesity, and dyslipidemia (6,7).

Recent evidence suggests that SUA contributes to oxidative stress, endothelial cell dysfunction, and systemic inflammation, all of which are critical factors in the progression of diabetic complications. Studies have demonstrated that elevated SUA levels are associated with increased oxidative stress markers, reactive oxygen species, and impairment in endothelial function. This dysfunction is often manifested clinically as albuminuria and elevated plasma endothelin levels, particularly in individuals with persistent hyperuricemia (8,9). Furthermore, hyperuricemia is no longer viewed solely as a precursor to gout, but as an independent risk factor associated with chronic kidney disease (CKD) and diabetic nephropathy. National data reveal that approximately 36% of individuals with T2DM in Pakistan exhibit hyperuricemia, highlighting the urgency of addressing this issue at a population level (10). Additionally, urate-lowering therapies have shown potential in decelerating the progression of CKD among hyperuricemic patients, further reinforcing the clinical relevance of SUA monitoring (11). Despite growing evidence, there remains a paucity of local data examining the relationship between SUA levels and diabetic nephropathy in T2DM patients within Pakistan. This study aims to determine the prevalence of elevated SUA levels in diabetic individuals and explore their association with diabetic nephropathy. If a significant relationship is established, routine monitoring of uric acid levels in diabetic patients may serve as a valuable tool in early identification of those at risk for nephropathy. Consequently, timely intervention with urate-lowering agents could be a cost-effective strategy to prevent or slow the progression of renal complications in this high-risk population.

METHODS

This descriptive cross-sectional study was conducted in the Department of Medicine at Khyber Teaching Hospital (KTH), Peshawar, over a six-month period from 1st September 2024 to 28th February 2025. A total of 139 male and female patients, aged 30 to 70 years, with a confirmed diagnosis of diabetic nephropathy were included. Both newly diagnosed and previously known cases of diabetes mellitus were eligible for inclusion. Diabetes was confirmed either by an HbA1c level greater than 6.5% or by a history of antidiabetic medication use for more than six months. Diabetic nephropathy was defined as a urinary albumin-to-creatinine ratio (UACR) exceeding 30 mg/g. Hyperuricemia was defined as a serum uric acid (SUA) level greater than 6.0 mg/dL. Participants were excluded if they had end-stage renal disease, hematologic disorders involving increased cell turnover, or were on medications known to influence uric acid metabolism (e.g., thiazide diuretics, allopurinol, febuxostat). The presence of other potential confounders such as hypertension, obesity, and dyslipidemia was not adjusted for in the analysis, which is acknowledged as a limitation. The sample size of 139 was calculated using the WHO sample size calculator based on prevalence data from prior literature (2,6). A non-probability convenience sampling technique was used to enroll patients from the outpatient department. The study received ethical approval from the Institutional Review

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Board of Khyber Teaching Hospital, Peshawar, and informed written consent was obtained from all participants after explaining the study's purpose, procedures, potential risks, and benefits.

Baseline demographic and clinical data were collected through a structured questionnaire, including variables such as age, gender, residence, occupation, education, monthly income, socioeconomic status, and duration of diabetes. Blood samples were drawn after a minimum fasting period of eight hours and analyzed for serum uric acid using the Selectra XL chemistry analyzer. All test results were reviewed and validated by a qualified pathologist to ensure accuracy and consistency. Data were entered and analyzed using SPSS version 20. Descriptive statistics were applied for both categorical and continuous variables. For continuous variables like SUA, fasting blood sugar (FBS), HbA1c, and UACR, normality was assessed using the Shapiro-Wilk test, and data were reported as mean ± standard deviation or median with interquartile range as appropriate. Categorical variables, including gender and hyperuricemia status, were expressed as frequencies and percentages. To examine associations between hyperuricemia and variables such as age, gender, residence, education, occupation, income level, and diabetes duration, post-stratification Chi-square or Fisher's exact tests were applied. A p-value <0.05 was considered statistically significant.

RESULTS

The study included 139 participants with diabetic nephropathy, comprising both males and females aged between 41 and 60 years. The mean age of participants was 50.20 ± 6.17 years. The average serum uric acid level recorded was 6.09 ± 1.74 mg/dL, while the mean body mass index (BMI) was 24.38 ± 2.71 kg/m². The mean weight and height of the study population were 71.32 ± 6.24 kg and 171.36 ± 7.75 cm, respectively. Out of the total participants, 119 individuals (85.6%) were above the age of 45 years, and 80 (57.6%) were male. A majority, 107 participants (77.0%), had a BMI greater than 24.0 kg/m². In terms of renal function staging, 66 patients (47.5%) had chronic kidney disease (CKD) stage above 3. Hyperuricemia, defined as serum uric acid level >6.0 mg/dL, was identified in 36 participants (26.0%). The remaining 103 individuals (74.0%) had uric acid levels within the normal range. Stratification of hyperuricemia with different variables revealed that among those aged ≤45 years, 30.0% had hyperuricemia, while among those aged >45 years, 25.2% were affected. Among males, the prevalence of hyperuricemia was 23.8%, compared to 28.8% in females. In participants with a BMI above 24.0 kg/m², 27.1% were hyperuricemic, while 21.9% of those with BMI ≤24.0 kg/m² were affected. Among patients with CKD stage above 3, 24.2% had hyperuricemia, compared to 27.4% of those with stage 3 or lower.

Statistical analysis showed no significant association between hyperuricemia and age group (p = 0.651), gender (p = 0.501), BMI (p = 0.544), or CKD stage (p = 0.672), indicating that hyperuricemia occurred independently of these baseline variables. The analysis revealed a strong and statistically significant positive correlation between serum uric acid levels and the degree of albuminuria, measured by urinary albumin-to-creatinine ratio (UACR), with a correlation coefficient of r = 0.949 and a p-value < 0.001. This suggests that higher uric acid levels are closely associated with more severe albuminuria, reinforcing the potential role of hyperuricemia in the progression of diabetic nephropathy. Furthermore, a similarly strong positive correlation was observed between serum uric acid levels and the duration of diabetes, with r = 0.955 and a p-value < 0.001, indicating that patients with longer-standing diabetes tend to have elevated uric acid levels. These findings highlight the importance of incorporating uric acid monitoring as a routine part of diabetes care, especially in patients with prolonged disease duration or early signs of nephropathy.

Table 1: Descriptive statistics of study participants according to various parameters (n = 139)

Parameters	Minimum	Maximum	Mean	Std. Deviation
Age (years)	41	60	50.20	6.166
Uric Acid(mg/dl)	2	9	6.09	1.738
Weight (kg)	56	88	71.32	6.239
Height (cm)	155	183	171.36	7.746
BMI (kg/m^2)	21.3	32.5	24.384	2.7069

Table 2: Baseline parameters of study participants (n = 139)

Parameters		Frequency	Percent
Age (years)	45 or below	20	14.4
	more than 45	119	85.6
Gender	Male	80	57.6

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Parameters		Frequency	Percent
	Female	59	42.4
BMI (kg/m^2)	24.0 or below	32	23.0
	more than 24.0	107	77.0
CKD stage	3 or below	73	52.5
	More than 3	66	47.5

Table 3: Stratification of hyperuricemia with various parameters (n = 139)

		Hyperuricemia		Total	P value
		No (n =103)	Yes (n = 36)		
Age (years)	45 or below	14	6	20	0.651
		70.0%	30.0%	100.0%	
	more than 45	89	30	119	
		74.8%	25.2%	100.0%	
Gender	Male	61	19	80	0.501
		76.3%	23.8%	100.0%	
	Female	42	17	59	
		71.2%	28.8%	100.0%	
BMI (kg/m^2)	24.0 or below	25	7	32	0.544
		78.1%	21.9%	100.0%	
	More than 24.0	78	29	107	
		72.9%	27.1%	100.0%	
CKD stage	3 or below	53	20	73	0.672
		72.6%	27.4%	100.0%	
	Above 3	50	16	66	
		75.8%	24.2%	100.0%	

Table 4: Correlation Analysis Results

Variables	Correlation Coefficient (r)	P-value
Uric Acid vs. UACR	0.949	0
Uric Acid vs. Duration of Diabetes	0.955	0

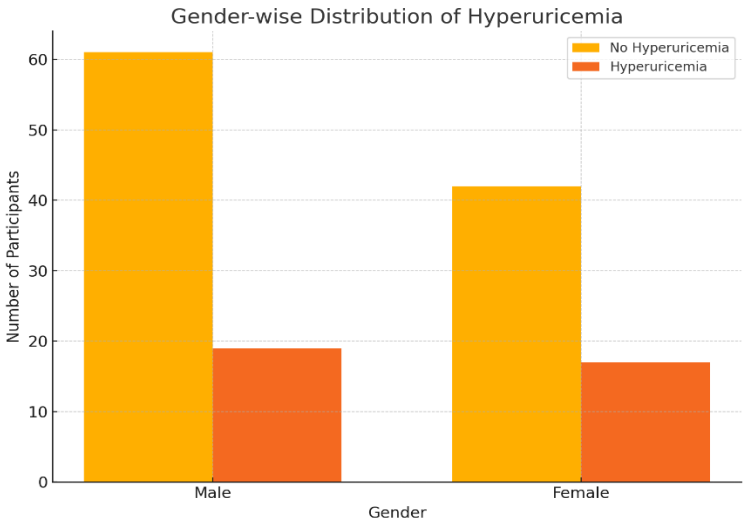

Figure 1 Gender-wise Distribution of Hyperuricemia

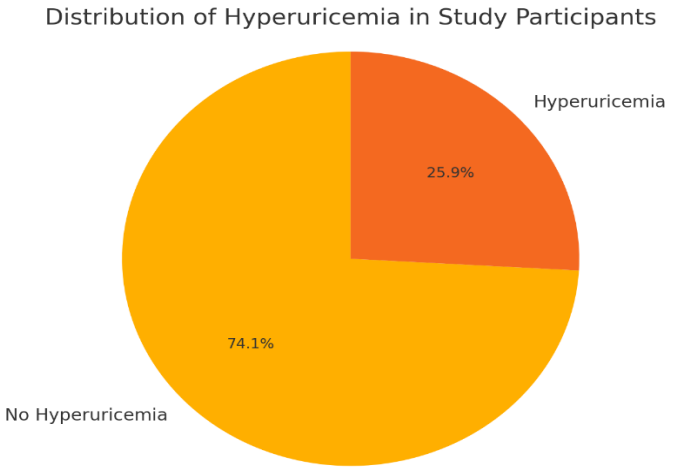

Figure 2 Distribution of Hyperuricemia in Study Participants

DISCUSSION

Serum uric acid (SUA) has emerged as a complex biomarker in the context of diabetes mellitus and its renal complications. Although it plays a physiological role as a major endogenous antioxidant, accounting for up to sixty percent of the plasma's free radical scavenging activity, persistently elevated levels have been linked with deleterious consequences, particularly in the kidneys (12). The current study demonstrated that approximately one in four patients with diabetic nephropathy had hyperuricemia, and strong positive correlations were observed between serum uric acid and both urinary albumin-to-creatinine ratio (UACR) and the duration of diabetes. These findings reinforce the growing body of evidence suggesting that SUA is not merely a metabolic byproduct but a potential mediator in the progression of diabetic kidney disease. Several earlier studies have proposed pathophysiological mechanisms linking elevated uric acid levels to renal damage. SUA has been shown to stimulate the renin-angiotensin system, induce pro-inflammatory cytokines, and impair endothelial nitric oxide availability, thereby promoting glomerular hypertension and interstitial fibrosis (13,14). In longitudinal observations, patients with elevated SUA progressed more frequently from microalbuminuria to macroalbuminuria and from normoalbuminuria to pathological urinary albumin excretion (15). These findings resonate with the present study's outcomes, where a clear association was found between higher SUA and increased albuminuria severity.

Evidence from population-based observational cohorts has previously suggested that hyperuricemia significantly increases the risk of developing diabetic nephropathy (16). Consistent with this, elevated SUA has also been linked to the onset of microalbuminuria, and its levels were found to correlate positively with HbA1c, suggesting a potential role of SUA in glycemic dysregulation and insulin resistance (17,18). A comparable trend was identified in studies conducted among patients with diabetic nephropathy, where SUA levels closely tracked the degree of albuminuria, reinforcing the role of uric acid as both a marker and mediator of renal injury (19,20). One of the key strengths of this study is the focused evaluation of serum uric acid within a well-defined population of patients with diabetic nephropathy, coupled with biochemical validation and standardized laboratory assessments. Additionally, the study addressed an important clinical gap by correlating SUA not only with hyperuricemia status but also with continuous clinical parameters such as albuminuria and diabetes duration, which are critical indicators of disease progression.

However, the study is not without limitations. The cross-sectional design precludes any determination of temporal or causal relationships between SUA and diabetic nephropathy. Potential confounders such as blood pressure, use of renin-angiotensin system inhibitors, and dietary purine intake were not accounted for, which may influence serum uric acid levels and kidney function independently. Moreover, the absence of renal histopathology or imaging-based assessments limits the ability to correlate biochemical findings with structural renal changes. The exclusion of longitudinal follow-up data also restricts the understanding of SUA dynamics over time in relation to renal outcomes. Future research should aim to incorporate prospective designs with broader adjustment for confounders, including metabolic syndrome components, antihypertensive and urate-lowering therapy use, and dietary factors. Genetic markers associated with

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uric acid metabolism and renal sensitivity to oxidative stress may further elucidate individual susceptibility patterns. Moreover, randomized controlled trials investigating the impact of uric acid-lowering therapies in delaying or reversing diabetic kidney disease could substantiate SUA as a modifiable therapeutic target (21). In conclusion, the present study substantiates the link between elevated serum uric acid and diabetic nephropathy, both in terms of urinary albumin excretion and disease duration. These findings highlight the potential clinical utility of routine SUA monitoring in diabetic patients to identify those at higher risk of renal deterioration, thus enabling earlier intervention and potentially improved renal outcomes.

CONCLUSION

This study concluded that hyperuricemia is notably associated with diabetic nephropathy in individuals with type 2 diabetes mellitus, supporting its role as a clinically relevant biomarker. Serum uric acid levels demonstrated potential as an accessible and informative tool for early identification of patients at risk for renal complications. Regular monitoring of uric acid, alongside other clinical and laboratory indicators, may aid in timely detection and intervention, thereby contributing to better management and possibly slowing the progression of diabetic kidney disease. These findings highlight the value of integrating serum uric acid assessment into routine diabetic care protocols.

AUTHOR CONTRIBUTION

Author	Contribution
Hanif Ullah Khan	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Inam Ullah Khan*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Zakir Khan	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Awais	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Yasin Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Siraj Ud Din	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Qaiser Wadud	Contributed to study concept and Data collection Has given Final Approval of the version to be published

REFERENCES

1. Jiang G, Luk AO, Tam CHT, Ozaki R, Lim CKP, Chow EYK, et al. Clinical Predictors and Long-term Impact of Acute Kidney Injury on Progression of Diabetic Kidney Disease in Chinese Patients With Type 2 Diabetes. Diabetes. 2022;71(3):520-9.
2. Pan J, Yang Q, Peng J, Li A, Liu Y, Yi B. A cohort study on the correlation between serum uric acid trajectory and the progression of renal function in patients with Type 2 diabetes mellitus. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2023;48(5):725-32.
3. Zou L, Wang Y, Qiu J, Yu R. Comment on "Is Uric Acid elevation a random finding or a causative agent of diabetic nephropathy?". Rev Assoc Med Bras (1992). 2020;66(7):1011.
4. Bai F, Li R. Comment on: Serum uric acid levels and diabetic kidney disease in patients with type 2 diabetes mellitus: A dose-response meta-analysis. Prim Care Diabetes. 2022;16(5):717.
5. Jiang J, Zhou X, Lan L, Weng J, Ren W. The correlation between serum uric acid and diabetic kidney disease in adult-onset type 1 diabetes patients in China. Acta Diabetol. 2023;60(9):1231-9.
6. Jiao X, Zhang G, Li G, Yin X, Shen X. Correlations of serum uric acid with glucose and lipid metabolism and renal function of type 2 diabetes mellitus patients. Panminerva Med. 2020;62(2):121-3.

7. Zhang J, Chen Y, Zou L, Jin L, Yang B, Shu Y, et al. Dose-response relationship between dietary antioxidant intake and diabetic kidney disease in the US adults with diabetes. Acta Diabetol. 2023;60(10):1365-75.
8. Zhu L, Sun J, Wang X, Tian R, Zhou Y, Yu J, et al. Elevated serum uric acid is not an independent risk factor for the occurrence of Type 2 diabetic kidney disease in Chinese populations. Medicine (Baltimore). 2022;101(50):e32128.
9. Lin Z, Zhang D, Zhang X, Guo W, Wang W, Zhang Y, et al. Extracellular status of thrombospondin-2 in type 2 diabetes mellitus and utility as a biomarker in the determination of early diabetic kidney disease. BMC Nephrol. 2023;24(1):154.
10. Zhang J, Chen Y, Zou L, Gong R. Prognostic nutritional index as a risk factor for diabetic kidney disease and mortality in patients with type 2 diabetes mellitus. Acta Diabetol. 2023;60(2):235-45.
11. Ji P, Zhu J, Feng J, Li H, Yu Q, Qin H, et al. Serum uric acid levels and diabetic kidney disease in patients with type 2 diabetes mellitus: A dose-response meta-analysis. Prim Care Diabetes. 2022;16(3):457-65.
12. Lovic D, Piperidou A, Zografou I, Grassos H, Pittaras A, Manolis A. The Growing Epidemic of Diabetes Mellitus. Curr Vasc Pharmacol. 2020 ;18(2):104-9.
13. Adnan M, Aasim M. Prevalence of type 2 diabetes mellitus in adult population of Pakistan: a meta-analysis of prospective cross-sectional surveys. Ann. Glob. Health, 2020;86(1):7.
14. An J, Nichols GA, Qian L, Munis MA, Harrison TN, Li Z et al. Prevalence and incidence of microvascular and macrovascular complications over 15 years among patients with incident type 2 diabetes. BMJ Open Diabetes Res Care, 2021;9(1):e001847.
15. Furuhashi M. New insights into purine metabolism in metabolic diseases: role of xanthine oxidoreductase activity. Am J Physiol Endocrinol Metab. 2020 Nov 1;319(5):E827-E834.
16. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA. Uric Acid and Oxidative Stress-Relationship with Cardiovascular, Metabolic, and Renal Impairment. Int J Mol Sci. 2022;16;23(6):3188.
17. Singh C, Jain S, Dhawan V, Kalra N, Kumari S. Uric acid as a predictor of endothelial dysfunction in patients with metabolic syndrome. Arch Endocrinol Metab. 2021;64(6):810-815.
18. Otaki Y, Konta T, Ichikawa K, Fujimoto S, Iseki K, Moriyama T et al. Possible burden of hyperuricaemia on mortality in a community-based population: a large-scale cohort study. Sci Rep. 2021;11(1):8999.
19. Ali G, Kamran MA, Amir M, Mumtaz B, Khan I, Tariq M. Frequency of Hyperuricemia in Type-2 Diabetes Mellites and its Relation with Diabetic Nephropathy. Pak. Armed Forces Med. J, 2023;73(1):199-203.
20. Wu N, Xia J, Chen S, Yu C, Xu Y, Xu C et al. Serum uric acid and risk of incident chronic kidney disease: a national cohort study and updated meta-analysis. Nutr Metab (Lond). 2021;18:1-0.
21. Sharma G, Dubey A, Nolkha N, Singh JA. Hyperuricemia, urate-lowering therapy, and kidney outcomes: a systematic review and meta-analysis. *Ther. Adv. Musculoskelet. Dis*, 2021;13:1759720X211016661.