

Effects of Bodybuilding Supplements on the Kidney: A Population-Based Biopsy Study among Middle Eastern Men

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Abstract

Background: The incidence of kidney diseases among bodybuilders is unknown.

Methods: Between January 2011 and December 2019, the Iraqi Kurdistan 15 to 39 year old male population averaged 1,100,000 with approximately 24,000 regular and 56,000 total gymnasium participants. In that period, 15 participants had kidney biopsies. Annual age specific incidence rates (ASIR) with (95% confidence intervals) per 100,000 bodybuilders were compared with the general age-matched male population.

Results: Among regular participants, diagnoses were: focal segmental glomerulosclerosis (FSGS), 2; membranous glomerulonephritis (MGN), 2; post-infectious glomerulonephritis (PIGN), 1; tubulointerstitial nephritis (TIN), 1; and nephrocalcinosis, 2. Acute tubular necrosis (ATN) was diagnosed in 2 newcomers and 5 regular participants. Anabolic steroids use was self-reported in 18%, protein powders in 71%, creatine in 29%, and veterinary grade vitamin D injections in 2.6% of regular participants. ASIR for FSGS, MGN, PIGN, and TIN among regular participants was not statistically different than the general population. ASIR of FSGS adjusted for anabolic steroid use was 5.1 (-0.2 to 12.3), a rate overlapping with FSGS in the general population at 2.0 (1.2 to 2.8). ATN presented with muscle pain and myoglobinuria among inexperienced bodybuilders and appeared secondary to exertional muscle injury. ASIR for ATN among total participants at 1.4 (0.4 to 2.4) was not considered significantly different than for the general population at 0.3 (0.1 to 0.5). Nephrocalcinosis was only diagnosed among bodybuilders at a 9-year cumulative rate of one per 314 vitamin D injectors.

Conclusions: Kidney disease rates among bodybuilders was not significantly different than for the general population, except for nephrocalcinosis that was caused by injections of veterinary grade vitamin D compounds.

Background

Weight training has become popular throughout much of the world, and it is estimated that 15–20% of United States (US) and European populations are members of gymnasiums [1]. Most gymnasiums sell supplements that typically consists of protein powders, creatine, and oral vitamins and minerals. Credible gymnasiums will not market anabolic steroids, but they are readily available in the outside community. The injection of subcutaneous and intramuscular high dose veterinary vitamin D and K compounds is practiced in South America and the Middle East with an apparently high frequency of end-stage renal disease (ESRD) [2,3].

A majority of competitive bodybuilders and weight athletes are likely to use anabolic steroids even though they are banned from most organized sports [4]. In 2013, the current superheavyweight Worlds Weight Lifting Champion and more than 100 other weight lifters from virtually every region of the world served bans after being tested positive for anabolic steroids [5]. Focal segmental glomerulosclerosis (FSGS) is frequently attributed to both anabolic steroids and excess protein intake [6,7,8]. Nevertheless, the scale of

the risk of FSGS, or any kidney disease, with bodybuilding supplements compared to the general population is currently undetermined.

The Kurdistan region in Northern Iraq has established nephrology practices and a centralized renal biopsy service [9]. We have developed a particular interest in supplement induced kidney injury, because several otherwise healthy young men have been identified with acute and chronic renal disease whose common background was a participation in gymnasium affiliated bodybuilding and the use of supplements [10]. This current population-based renal biopsy study estimates the incidence of specific diagnoses of renal disease among bodybuilders and compare the incidence to age matched, biopsy-defined kidney disease in the general population.

Methods

Patients, who were residents of Sulaimania, Erbil, or Dohuk were biopsied because of an elevated serum creatinine and/or proteinuria. All biopsies were studied by light microscopy in 18 serial sections using hematoxylin and eosin, periodic acid-Schiff, Masson trichrome, and Jones methenamine silver stains, and by immunofluorescence microscopy with fluorescein conjugated anti-human IgG, IgM, IgA, C3, C1q, and albumin. Electron microscopy was not performed on any of the bodybuilding cases.

The study was observational for two defined periods of time. One for body builders and one for the general population. This was because of the disparity in the number of cases in each group. The inclusion criteria were a renal biopsy for both groups and there were no exclusion criteria. Therefore, this was not a cross-sectional, case-control, or a cohort-study but an analysis of existing data in our regional kidney biopsy repository and would not fall under STROBE guidelines. Nevertheless, the STROBE reporting checklist for cross-sectional studies was followed for items that seemed appropriate. This includes the methods of estimating population sizes and precision estimates of quantitative variables.

The number of regional bodybuilders was tabulated from 2019 client registration lists by managers of gymnasiums in Erbil, Sulaimania, and Dohuk and extrapolated to the number of gymnasiums registered in 2015 by the Kurdistan Regional Government Licensing Committee. The gymnasium registrations were divided into two categories. Category A: all registrants. Category B: regular registrants who continued participation after one year. For the year 2015, all registrants were estimated at 56,000 and regular registrants at 24,000. The ages of 94% of the clients were between 18 and 39 years old.

The annual age specific incidence rate (ASIR) of kidney biopsy diagnoses per 100,000 males among the general Kurdistan population was calculated for the two year period 2012–2013 as previously reported [9]. An estimate of the Kurdistan population at 4,900,000 persons was derived from 2011–2012 United Nations Iraq population data and the 2012 Iraqi Cancer Registry [11]. The estimated number of males between 15 to 39 years of age was 1,100,000.

Kidney biopsies were obtained on 15 bodybuilders over a 9.0 year period from January 1, 2011 to December 31, 2019. The annual ASIR of kidney biopsy disease diagnoses per 100,000 bodybuilders was

calculated from 24,000 regular participants for FSGS, membranous glomerulonephritis (MGN), post-infectious glomerulonephritis (PIGN), tubulointerstitial nephritis (TIN), and nephrocalcinosis. For acute tubular necrosis (ATN), ASIR was calculated from all participants at 56,000, because not all ATN patients were regular participants. ASIR for bodybuilders was compared with the rates of disease in the general population in the years 2012–2013. Because of the small number of bodybuilding cases, the aggregate age range of 15 to 39 years was used to calculate ASIR for both bodybuilders and the general population. The 95% confidence intervals (95% CI) of the ASIR was calculated as: $95\% \text{ CI (ASIR)} = 1.96x(\sqrt{Ri^2/Ni})$; where, Ri = age-specific incidence in the 15–39 year old age group and Ni = number of biopsies in the 15–39 year age group [12]. Differences in ASIR were considered significant if the 95% CI do not overlap.

Results

Renal biopsies

The clinical and biopsy findings and supplement use of the 15 bodybuilders are summarized in Table 1. The diagnoses consisted of two cases of FSGS, two cases of MGN, one case of PIGN, one case of TIN, two cases of nephrocalcinosis, and seven cases of ATN. Thirteen of the 15 subjects were regular participants with two to more than 20 years experience.

Two of the seven patients (patients 6 and 7) with ATN presented with a history of muscle pain at one and 6 months after beginning bodybuilding. These patients are considered newcomers to bodybuilding and not regular participants. Patient 6 had taken protein supplements only and patient 7 took no supplements. Serum creatinine levels were 8.6 mg/dL (patient 6) and 3.8 mg/dL (patients 7). Serum creatinine kinase was 6893 U/L for patient 6 and 1254 U/L for patient 7. Both had immunohistochemically demonstrated myoglobin casts in their biopsies. Five of the seven ATN patients had been bodybuilding from two to seven years and presented with afebrile malaise with serum creatinine levels from 2.6 to 3.8 mg/dL. All five had used anabolic steroids, protein powders, and creatine supplements. The biopsies of these five ATN patients showed intratubular microcalcifications associated with foci of degenerating and regenerating tubular epithelium (Figure 1) but with no myoglobin casts.

Five of the seven ATN biopsies revealed evidence of chronic injury with 15–40% interstitial fibrosis and tubular atrophy. Serum creatinine levels returned to normal in all ATN patients, including those with histologic chronicity. The clinical ATN events occurred during the summer in four patients and during the winter in three patients, and all training took place in air conditioned gymnasiums.

The patient with TIN used protein and creatine supplements but not anabolic steroids. His kidney biopsy revealed lymphocytic and plasma cell infiltrates but without eosinophils. He had no pyelographic evidence of reflux, and his biopsy showed minimal chronicity. The renal failure resolved when creatine and protein supplements were discontinued

Patients 14 and 15 injected veterinary grade vitamin D compounds. The products were 100 ml solutions containing 50,000,000 IU of vitamin K, 7,000,000 IU of vitamin D, and 5,000 IU of vitamin E in a sesame oil

base. The kidney biopsies demonstrated nephrocalcinosis with extensive intratubular and interstitial calcium deposits and advanced interstitial fibrosis and tubular atrophy (Figure 2). One of these patients progressed to end-stage renal disease (ESRD) and kidney transplantation shortly after biopsy.

Soft tissue was removed from the shoulder, chest, and arm injection sites of the two patients with nephrocalcinosis. This tissue showed lipogranulomatous inflammation with large calcium deposits (Figure 3). When the soft tissue was removed 20 months after the kidney biopsy of patient 15, serum calcium was 12.8 mg/dl (normal range 8.5 to 10.5 mg/dl) and serum vitamin D was 158 ng/ml (normal range 30–80 ng/ml). At the last clinic visit, patient 15 had a serum creatinine of 3.4 mg/dl. At a body weight of 84 kg, the Cockcroft-Gault eGFR was 36 ml/min/1.73m².

The biopsy of patient 9, a 30 year old, with FSGS showed a not otherwise specified pattern with more than 50% interstitial fibrosis and tubular atrophy. He required transplantation 36 months following the diagnosis. The biopsy of the patient 10, a 40 year old, with FSGS demonstrated perihilar glomerulosclerosis with hyalinosis in one of 8 glomeruli and no interstitial fibrosis or tubular atrophy. This patient was a competitive bodybuilder with a 20 year history of anabolic steroid and protein supplement use. His body mass index (BMI) was 33.6. At the time of biopsy, serum creatinine was 1.3 mg/dl with a body weight adjusted Cockcroft-Gault eGFR of 108 ml/minute. Urine protein was 1+ by Uripath™ dipstick testing and was not further quantitated. Serum creatinine levels were 1.2 and 1.3 mg/dL one year after the biopsy.

The biopsies of two patients with MGN were consistent with a primary disease. Serological testing for ANA and dsDNA were negative; Antibodies for anti-phospholipase A2 testing were not available. The patient with PIGN show no signs of any injection site infection, and cardiac ultrasonography showed no valvular disease.

Incidence estimates of kidney disease diagnoses among body builders

Questionnaires completed by 150 regular gymnasium participants recorded the following supplement usage: Anabolic steroids, 18%; protein powders, 71%; creatine, 29%; injected high dose veterinary vitamin D, 2.6%. The anabolic steroid use consisted of combinations of stanozolol and nandrolone in 5%, testosterone propionate/cypionate and stanozolol/nandrolone in 5%, and a single agent either testosterone or nandrolone in 8%.

Table 2 shows the ASIR of renal biopsy diagnoses among bodybuilders in which the annual biopsy rate was 6.9 per 100,000 regular participants. For regular participants, ASIR for FSGS, MGN, and nephrocalcinosis was 0.9 (−0.4 to 2.2), and for PIGN and TIN, ASIR was 0.5 (−0.4 to 1.4). The ASIR for FSGS, MGN, PIGN, and TIN were similar to those for the general population (Table 3) with broad overlapping of the 95% CI indicating an absence of statistically significant differences. When adjusted for the 18% of anabolic steroid use, the ASIR of FSGS among body builders was 5.1 (−2.0 to 12.3).

Nevertheless, an absence of statistical significance was reflected in the wide 95% CI that overlapped the incidence of FSGS in the general population at 2.0 (1.2 to 2.8). The annual biopsy rate in the general population for the diseases found among body builders was 3.4 per 100,000 15 to 39 year old males.

Nephrocalcinosis was found only among bodybuilders and was identified in two patients. When adjusted for the 2.6% of body builders that injected vitamin D, the ASIR for nephrocalcinosis was 35.3 (0.7 to 69.8) per 100,000 vitamin D injectors.

Because two patients with ATN were newcomers to bodybuilding, the ASIR for ATN was calculated from the number of all gymnasium registrants at 1.4 (0.4 to 2.4). The upper level of the 95% CI of ASIR for ATN in the 15 to 39 year old general male population at 0.3 (0.1 to 0.5) overlapped the lower limit of the 95% CI of ASIR of ATN for bodybuilders. This is interpreted as an absence of evidence that the frequency of ATN was different for the two groups.

Discussion

Among these Iraqi Kurdistan bodybuilders, renal disease rates, except for nephrocalcinosis, were similar to those found in the age-matched, general male population. Nephrocalcinosis was a uniquely bodybuilding disease and was found only with injections of veterinary grade vitamin D compounds. It did not occur in everyone using veterinary compounds but had an estimated 9-year cumulative occurrence of one per 314 vitamin D injectors. Of the two nephrocalcinosis patients in this study, one required transplantation, and the other, one year after diagnosis, had moderately advanced, although apparently stable, chronic kidney failure. The absence of clinical disease in the majority of vitamin D injectors and the stability of disease in one of our patients suggests that nephrocalcinosis might be manageable or even avoidable with early intervention. For the level of anabolic steroid use practiced in the region, that includes multiple drugs simultaneously in 10% of bodybuilders, the frequency of FSGS among bodybuilders could not be considered any greater than the general population risk.

ATN was the most common type of renal disease encountered among our bodybuilders and occurred at an annual rate of one per 71,000 gymnasium participants. Acute kidney injury (AKI) in the developing world is a major current interest in nephrology, particularly among the young, because it identifies a group that may have preventable disease [13].

We commonly see elevated creatinine levels in laborers and soldiers during the summer months, but AKI in these as well as trauma patients is treated on the basis of clinical findings and laboratory chemistries, and patients are not biopsied. Patients with evidence of AKI are biopsied if there is no apparent underlying cause, and these biopsied patients represent our estimates of the incidence of ATN in our general 15–39 year old male population. Among the bodybuilders with ATN, the elevations in creatinine were substantial, averaging 4.1 mg/dL and ranging from 2.6 to 8.6 mg/dL, values well above the lower criteria for AKI in KDIGO Clinical Practice Guidelines [14].

Data on the rates of AKI for young males is not readily available, but the 1996 study by Liano et al. [15] may provide a rough estimate of this frequency. These authors report an annual clinical incidence for ATN of 8.8 patients per 100,000 persons who were admitted at an average of 63 ± 17 years of age to hospitals in the Madrid region of Spain. If the proportion of AKI patients under 44 years old is 21% and the proportion with no associated disease is 50% as reported by Shawney et al. [16], the incidence of ATN for 34 young patients with no comorbid disease would be approximately 0.9 (0.6 to 1.2) patients per 100,000 Madrid residents [15]. This is higher than the biopsy incidence of ATN at 0.3 (0.1 to 0.5) per 100,000 among the general Kurdish male population but also indicates that biopsy determinations of ATN underestimate its clinical incidence.

Two of the ATN patients we report recently began bodybuilding and presented with muscle pain and evidence of rhabdomyolysis. Muscle pain commonly occurs with new weight lifting regimens and is attributed to microscopic muscle damage [17,18]. This is referred to as exertional muscle injury and is usually accompanied by elevations in serum creatine kinase [18]. Less commonly myoglobin is elevated, with the latter marker being of particular concern because of its association with kidney injury [18]. In the new bodybuilders, ATN may have been the result of excessive muscle damage resulting from overexertion for the person's level of training.

Muscle pain was not acknowledged by patients with ATN who were regular bodybuilding participants. The cause of this kidney injury is obscure, and it is uncertain whether their ATN is related to bodybuilding or part of an unidentified AKI occurring in the general community. The biopsies of ATN among these more experienced bodybuilders contained microcalcifications, and all patients consumed commercial vitamin and mineral capsules as well as protein and creatine powders. Nevertheless, all of this consumption was well within amounts that, individually or together, are not known to adversely affect kidney function [19,20,21]. It is likely that microcalcifications were the result of dystrophic calcification of cells damaged by a previously unknown insult and not an indication of a primary role of calcium in the kidney injury [10]

While patients with ATN in our current study presented as acute renal insufficiency, most had histologic evidence of chronic injury suggesting prior kidney damage. Patients with community acquired AKI have up to three times the rate of ESRD as the general population, with the ESRD being primarily related to advanced age and high rates of cardiovascular disease. [22,23]. Whether the risk applies to younger patients is not clear, but baseline normal renal function associates with a decreased risk of ESRD over time [23,24]. This implies that the prognosis in otherwise healthy young men will not be compromised if the injury is not repeated.

In some cases, the pathology underlying the AKI in bodybuilders has been a TIN resembling a drug-type allergy in which the renal failure resolves when supplements are discontinued [25,26]. This TIN is uncommon and, in the current study, occurred at an annual rate of 1 per 200,000 gymnasium users, a frequency not different than TIN in the general population.

FSGS has been linked to anabolic steroid use, and there is experimental evidence that anabolic steroids may be toxic to podocytes [6,7,8]. While this suggests a mechanism of injury, the primary association

between anabolic steroids and FSGS, comes from case studies and particularly the 2011 report by Herlitz et al. [7] of six white and four Hispanic bodybuilders or power lifters aged 28 to 45 years old that developed FSGS after years of training that included using multiple anabolic steroids. This cohort consisted of nine patients from New York City (NYC) and one from Boston that was collected over a 10 year period at three major reference centers and presumably reflects the collective experience of nephrologists and pathologists in the region.

The use of anabolic steroids among males in NYC is probably similar to the 2–4% that is estimated for the US as a whole [27,28]. In this case, the population of anabolic steroid users in the 2011 NYC population of 1.65 million males 20–49 years old would be approximately 31,400 [29]. The nine NYC patients in the paper by Herlitz et al. (7) would then calculate to an annual ASIR of 2.9 (1.0 to 4.8) patients per 100,000 steroid users.

The diagnosis of FSGS has been increasing over the last 20–30 years, and FSGS is now the major cause of nephrotic syndrome in the US and in several other parts of the world, including Iraq [9,30,31]. The incidence of FSGS has been estimated from biopsy series from the Mayo Clinic for Olmstead County, Minnesota and from Melbourne, Australia [32,33].

The FSGS estimate of 2.9 (1.0 to 4.8) per 100,000 NYC body builders may indicate an increased risk when compared to the all age and both gender FSGS incidence of 1.1 (0.7 to 1.5) per 100,000 persons in Olmstead County [32]. It does not indicate a significantly increased risk when compared to the FSGS rate of 1.9 (1.3 to 2.5) per 100,000 white males 25–44 years old in Melbourne [33]. A 2009 health assessment for the National Football League (NFL) surveyed 1,625 former players and did not find any excess of renal disease [34]. This group of athletes were known to frequently use anabolic steroids, particularly those retiring prior to the implementation of NFL anti-doping policies in 1989 [35].

The difficulty of making a comparison between the patients in the study by Herlitz et al. [7] and most athletes is that the NYC bodybuilders could be considered steroid dependent, a condition estimated to afflict about 30% of anabolic steroid users [27,28]. It is not at all clear whether the FSGS anabolic steroid risk should be based upon all users or only those that are considered dependent. Although the number of patients may be too small for the detection of rare kidney events, clinical studies of dependent anabolic steroids users have found “accelerated” coronary atherosclerosis and left ventricular muscle dysfunction but have not mentioned renal disease [27,28]. Nevertheless, if FSGS is increased among US anabolic steroid users, dependent or otherwise, the frequency of its recognition seems disproportionately low compared to the high rates of anabolic steroid exposure in US athletic communities [4,27,28]. In a 2019 scientific statement, the Endocrine Society recognized FSGS as a complication of anabolic steroid use, but considered it uncommon and less serious than cardiovascular disease [28].

Nearly all of the reports of nephrocalcinosis complicating bodybuilding have come from Brazil (2,3), but the use of up to 10,000 units a day of vitamin D is recommended in US and European muscle building e-magazines as a “steroid” that enhances muscle development [36,37]. With this level of advocacy, it is difficult to understand why nephrocalcinosis among bodybuilders appears to be so regionally localized, but

it may be the method of delivery and the inflammatory response to the injections that contributes to the kidney disease.

The oil-based veterinary compounds are inexpensive and mainly used to add bulk to specific muscle groups. As was found in patient 15, the granulomatous oil containing reaction can act as a slowly releasing reservoir for the lipid soluble vitamins for months and possibly years [38]. While the injection of high-dose veterinary vitamin compounds does not seem to have any role in Western bodybuilding, some European bodybuilders inject paraffin oils around muscles for their contouring effect, a practice that is also seen in some cosmetic surgeries [39,40]. The oils elicit a granulomatous reaction that is associated with hypercalcemia as a result of the local synthesis of active vitamin D [39,40]. Renal failure that is corrected when calcium and vitamin D levels are lowered is reported in most of these patients [39,40].

A major difficulty with the current study is that kidney disease was uncommon among gymnasium participants. This is inherent in the evaluation of any type of rare population event [12]. FSGS is a useful example because of its controversial association with anabolic steroids. We estimate that a relationship between FSGS and anabolic steroids in our region would have required the identification of six FSGS patients over the 9.0 year collection period to be considered significantly different than its usual population frequency (Table 4). The threshold of six patients is needed despite what appears to be marked increases in ASIR with a simulated increase of even three or four FSGS patients.

The calculations emphasize that comparisons of the frequency of rare events that are typical of most kidney diseases can be misleading and require a measure of statistical uncertainty. In population studies, this uncertainty is usually achieved by confidence intervals, but because rare events produce very wide confidence intervals, the relevance of the estimates is frequently difficult to understand [12].

It is also a concern that our interest in bodybuilding-related kidney disease may have created an investigative bias, as the biopsy frequency for regular gymnasium participants was more than twice that of the general population. Since, however, the different biopsy frequencies uncovered essentially the same rates of disease, it is likely that, except for nephrocalcinosis, the kidney health of bodybuilders is not worse than that of other young men in the region.

Conclusion

Young middle-Eastern men participate in bodybuilding and consume supplements including anabolic steroids like their counterparts in the US and Europe. In this population-based biopsy study, we found that the frequency of kidney disease among Kurdistan Iraqi bodybuilders as measured by age-specific incidence rates was not significantly different than the age matched general population with one important exception. Persons who injected veterinary grade vitamin D compounds for their muscle contouring effect assumed a high risk of end-stage kidney disease. These injections have been recently introduced into the region and enjoy some popularity. The practice is not condoned by gymnasium trainers or managers and needs to be addressed by health authorities as having substantial morbidity and potential mortality.

List Of Abbreviations

FSGS, focal segmental glomerulosclerosis; MGN, membranous glomerulonephritis; TIN, tubulointerstitial nephritis; PSGN, post-streptococcal glomerulonephritis; ATN, acute tubular necrosis; AKI, acute kidney injury; ASIR, age standardized incidence rate; 95% CI, 95% confidence intervals; ESRD, end-stage renal disease; IF/TA, interstitial fibrosis and tubular atrophy; NYC, New York City; NFL, National Football League.

Declarations

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Competing interests

None to declare.

Availability of data and materials

Compiled data and calculations are stored in Excel files in the Shorsh University Hospital Pathology Department and will be made available upon request to the corresponding author MDH.

Authors contributions

Study design and concepts: AAA, SEA, DAS, MDH. Data collection and analysis: AAA, SEA, DAS, ZSMS, MDN. First draft of manuscript: AAA, MDH. MDH coordinated manuscript revisions that were read and approved by all authors.

Consent for publication

Written informed consent was obtained from patients for case descriptions and for the accompanying images..

Ethics approval and consent to participate

The Ethics and Research Review Committee of Sulaimania University gave permission for the research. The research was conducted according to the Helsinki Accords. The research was a review of existing medical and pathology records. It involved no additional patient intervention or approval.

Conflict of Interest Statement

The authors declare no conflict of interest. The manuscript has not been previously published in whole or in part.

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Tables

Table 1. Clinical characteristics and pathology of regional body builders undergoing renal biopsies.

Patient no.	Age	Duration of training	Pathology diagnosis	IF/TA	AS	protein	creatinine	Vit D	1 year S[Cr]
1	26	7 years	ATN, microcalcifications	30%	+	+	+	Oral	1.3
2	21	3 years	ATN, microcalcifications	15%	+	+	+	Oral	1.0
3	21	4 years	ATN, microcalcifications	0	+	+	+	Oral	1.1
4	20	3 years	ATN, microcalcifications	40%	+	+	+	Oral	1.2
5	23	2 years	ATN, microcalcifications	20%	+	+	+	Oral	1.2
6	22	6 month	ATN, myoglobin casts	30%	-	+	-	-	1.0
7	19	1 month	ATN, myoglobin casts	0	-	-	-	-	1.0
8	30	5 years	TIN	10%	-	+	+	Oral	1.1
9	30	10 years	FSGS, NOS	50%	+	+	+	Oral	ESRD, Tx
10	40	20+ years	FSGS, perihilar (1 of 8 glomeruli)	0	+	+	+	Oral	1.3
11	32	8 years	PIGN	0	+	+	+	Oral	1.2
12	49	20+ years	MGN	5%	+	+	+	Oral	1.1
13	26	5 years	MGN	25%	+	+	+	Oral	1.3
14	27	8 years	Nephrocalcinosis	70%	+	+	+	INJ	ESRD, Tx
15	24	2 years	Nephrocalcinosis	40%	+	+	+	INJ	3.4

Abbreviations: S[Cr], serum creatinine; AS, anabolic steroids; ATN, acute tubular necrosis; FSGS, focal segmental glomerulosclerosis; PIGN, post-infectious glomerulonephritis; MGN, membranous; glomerulonephritis; TIN, tubulointerstitial nephritis; INJ, injected veterinary grade Vitamin D compounds.

Table 2. Age specific incidence rate (ASIR) of kidney disease diagnosed among bodybuilders in Kurdistan of Iraq in the 9 year period from January 1, 2011 through December 31, 2019.

diagnosis	biopsies 9.0 yrs	Annual average	Pop at risk	ASIR	95% CI	ASIR by suppl	95% CI by suppl
FSGS	2	.22	24,000	0.9	-0.4 to 2.2	5.1	-2.0 to 12.3
MGN	2	.22	24,000	0.9	-0.4 to 2.2		
PIGN	1	.11	24,000	0.5	-0.4 to 1.4		
TIN	1	.11	24,000	0.5	-0.4 to 1.4		
ATN	7	.78	56,000	1.4	0.4 to 2.4		
nephrocalcinosis	2	.22	24,000	0.9	-0.4 to 2.2	35.3	0.7 to 69.8

ASIR was calculated per 100,000 body builders for all diagnoses and adjusted by specific supplement use for FSGS (anabolic steroids, 18%) and nephrocalcinosis (injected vitamin D, 2.6%). The population at risk for bodybuilders was considered to be regular participants at 24,000 except for ATN in which the population at risk was considered to be all participants at 56,000.

Table 3. Age specific incidence rate (ASIR) of kidney disease diagnosed among the male general population of Kurdistan of Iraq aged 15 to 39 years old in the two years period 2012-2013.

diagnosis	biopsies 2 yrs	Annual average	Pop at risk	ASIR	95% CI
FSGS	45	22.5	1,100,000	2.0	1.2 to 2.8
MGN	17	8.5	1,100,000	0.8	0.3 to 1.3
PIGN	2	1	1,100,000	0.1	0.0 to 0.2
TIN	7	3.5	1,100,000	0.3	0.0 to 0.6
ATN	6	3	1,100,000	0.3	0.1 to 0.5
Nephrocalcinosis	0	0	1,100,000	0	

ASIR was calculated per 100,000 males.

Table 4. Projected age specific incidence rates (ASIR) for focal segmental glomerulosclerosis with increasing numbers of biopsy diagnoses.

diagnosis	biopsies 9 yrs	Annual average	Pop at risk	ASIR	95% CI
FSGS steroid users	2	0.22	4320	5.1	-2.0 to 12.3
"	3	0.33	4320	7.7	-1.0 to 16.4
"	4	0.44	4320	10.3	0.2 to 20.4
"	5	0.56	4320	12.9	1.6 to 24.1
"	6	0.67	4320	15.4	3.1 to 27.8
FSGS gen population	-	22.5	1,100,000	2.0	1.2 to 2.8

Rates are for anabolic steroid using bodybuilders are compared with FSGS rates in the male general population of Kurdistan of Iraq aged 15 to 39 years for the years 2012-2013. ASIR is calculated per 100,000 males.

Figures

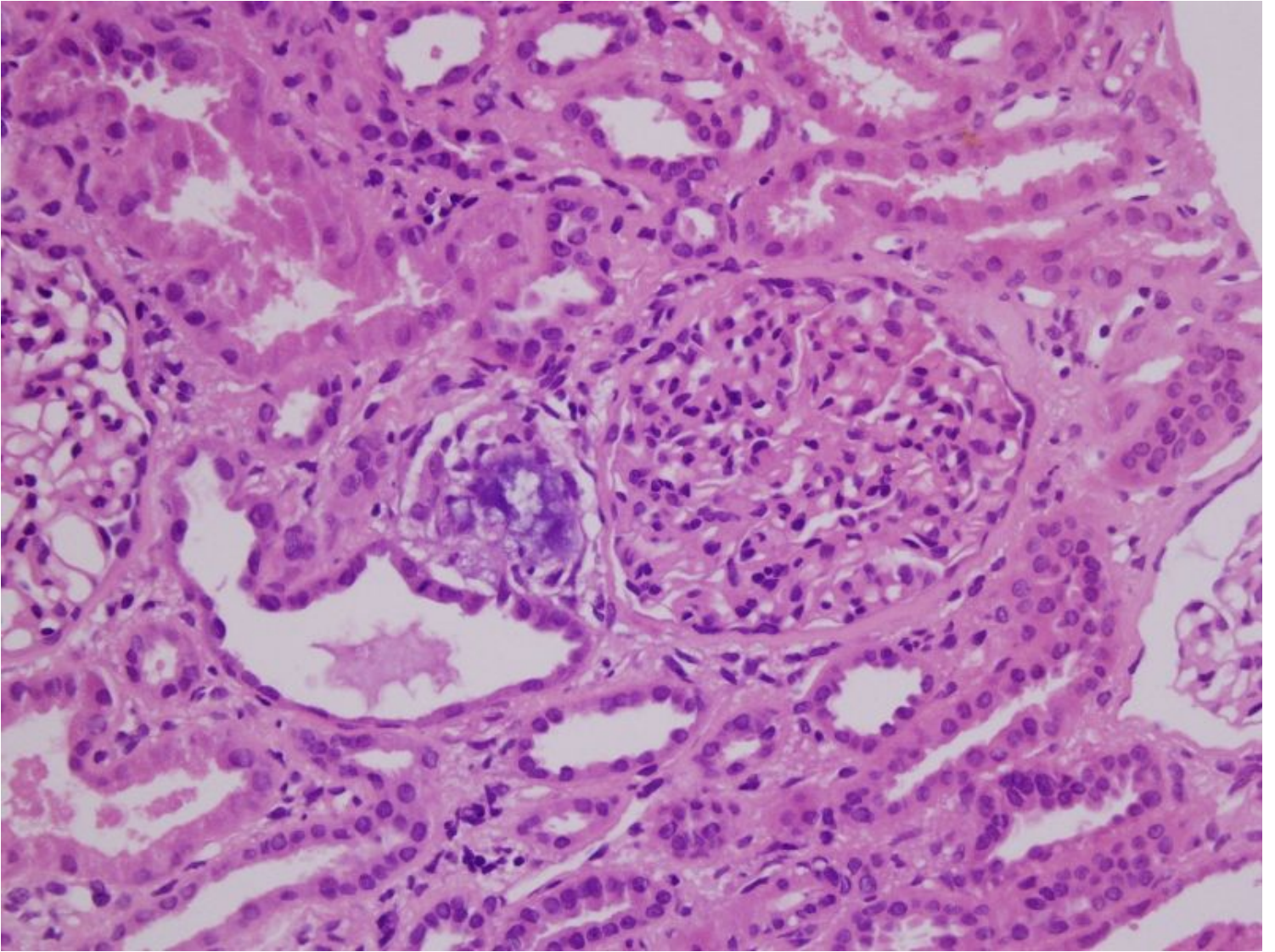


Figure 1

Patient 1. A 26 year old who had been training for 36 months. He presented with renal insufficiency and a creatinine of 2.6 mg/dl. The biopsy shows dilated tubules lined by flattened mitotically active epithelium. An intraluminal calcification surrounded by regenerative cells is present. Hematoxylin and eosin stain x400.

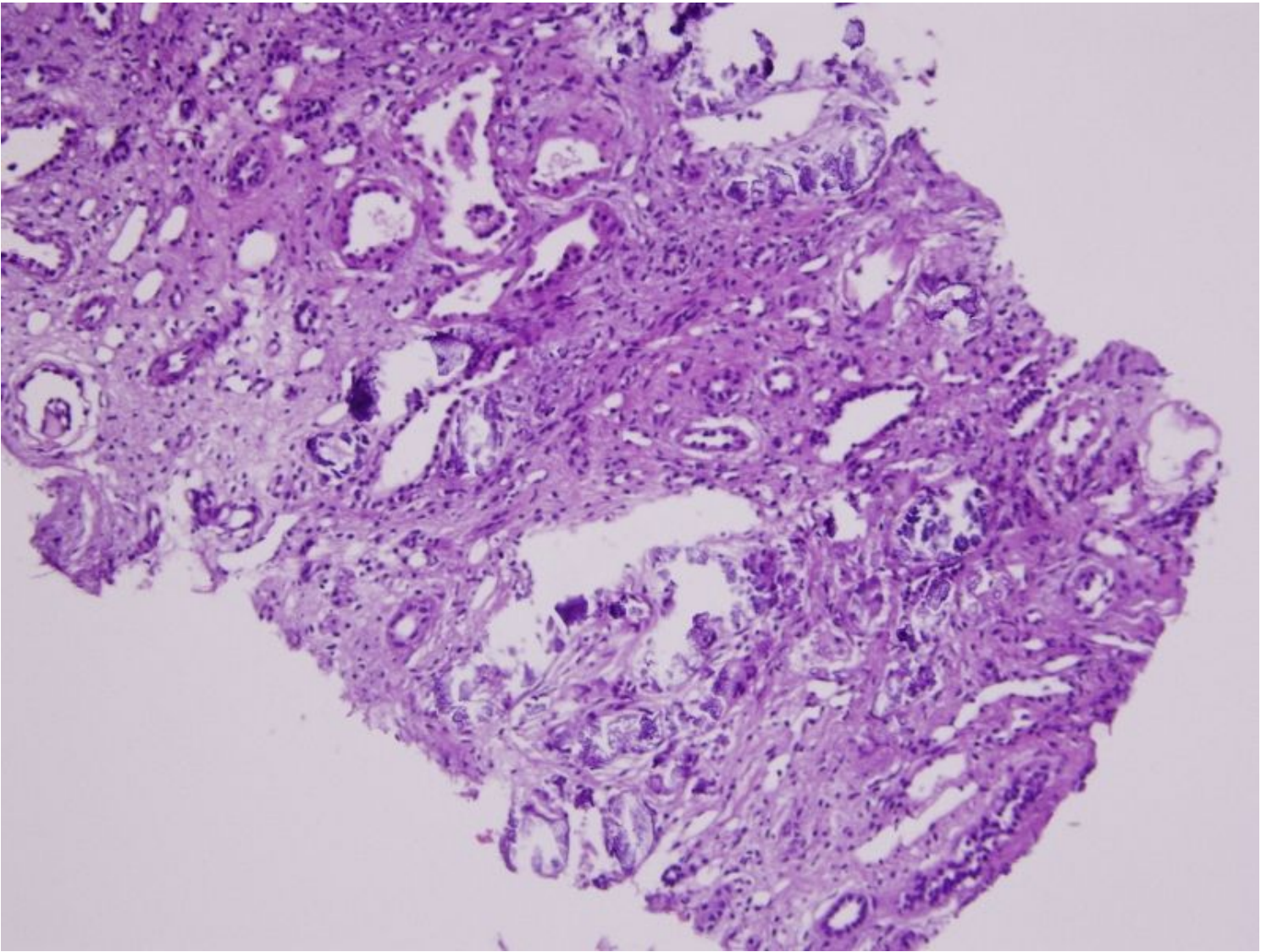


Figure 2

Patient 14. A 27 year old competitive body builders who injected veterinary grade vitamin compounds. The biopsy shows massive tubular and interstitial calcium deposits with advanced interstitial fibrosis and tubular atrophy. He required transplantation shortly after the biopsy. Hematoxylin and eosin stain x100.

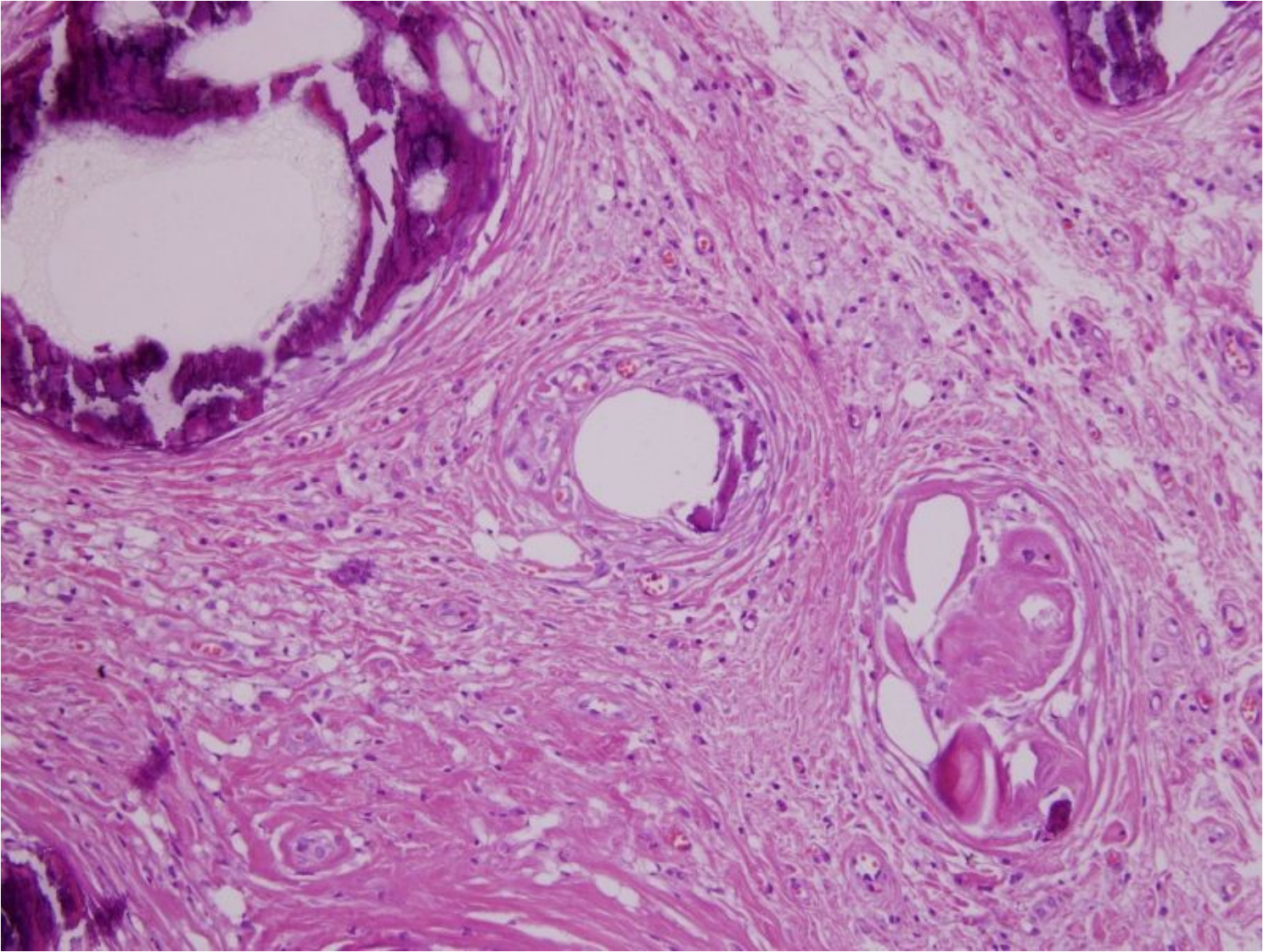


Figure 3

Patient 15. Soft tissue removed from veterinary grade vitamin injection sites in the shoulder of a 24 year old bodybuilder. The soft tissue was removed 20 months after a kidney biopsy showed nephrocalcinosis. At this 20 month interval, he was hypercalcemic and had hypervitaminosis D. The serum creatinine had increased to 3.4 mg/dl from 1.9 mg/dl at the time of his renal biopsy. The tissue demonstrates calcifications and lipogranulomatous inflammation surrounding oil droplets. Hematoxylin and eosin stain x100.