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EVALUATION OF VARIATIONS IN BLOOD AND LIVER BIOCHEMICAL PARAMETERS IN BODYBUILDERS USING CREATINE SUPPLEMENTS

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR
THE DEGREE OF MASTER OF SCIENCE
IN
CHEMISTRY

BY

BASSAM WATHEQ ABDULATEEF AL-SHAMMARI

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By Bassam Watheq Abdulateef AL-SHAMMARI

April 2023

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

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Bassam Watheq Abdulateef AL-SHAMMARI

ABSTRACT

EVALUATION OF VARIATIONS IN BLOOD AND LIVER BIOCHEMICAL PARAMETERS IN BODYBUILDERS USING CREATINE SUPPLEMENTS

Bassam Watheq Abdulateef AL-SHAMMARI

Master of Science in Chemistry

Advisor: Assoc. Prof. Dr. Şevki ADEM

April 2023

The clinical and demographic characteristics of thirty people who took creatini in IRQI gym were studied. Nutrition supplementation is more common in those under 35. Our research found no significant differences in age mean and SD in three groups (group 1=29.34.3.66, group 2=28.44.4.19), Chi sequre = 0.50, DF= 2, P= 0.77. Your study found a strong BMI association between obese and non-obese people. 26 out of 30 people were obese (86%) whereas 4 out of 30 had a normal BMI (14%). The serum creatnin levels of those who used creatine supplements were higher than usual (p0.01). (6331109.11) and (197.02), respectively, relative to the normal sample. urin creatnine supplemented subjects had higher levels than healthy controls (P 0.01). Group 1 had an average of 633109.11 and Group 3 had 197.02. 0.001 With and without creatine supplementation, mean levels have considerable (p 0.001). GROUP 1 = 160.5420.67, GROUP 2 = 87.3810.15) vs. normal sample (GROUP 3 = 70.1812.91). AST, ALT, ALP, Total protein, and albumin may be changed by creatine supplementation.

2023, 47 pages

Keywords: Creatinine clearuce, Creatine, Bodybuilders, Effects of creatine, Nutritional supplements

ÖZET

KREATİN TAKVİYESİ KULLANAN VÜCUT GELİŞTİRİCİLERDE KAN VE KARACİĞER BİYOKİMYASAL PARAMETRELERİNDEKİ DEĞİŞİKLİKLERİN DEĞERLENDİRİLMESİ

Bassam Watheq Abdulateef AL-SHAMMARI

Kimya, Yüksek Lisans

Tez Danışmanı: Doç. Dr. Şevki ADEM

Nisan 2023

IRQI spor salonunda kreatini alan otuz kişinin klinik ve demografik özellikleri incelenmiştir. Beslenme takviyesi 35 yaşın altındakilerde daha yaygındır. Araştırmamız üç grupta (grup 1=29,34,3,66, grup 2=28,44,4,19), yaş ortalaması ve SD açısından anlamLı bir farklılık bulmadı, Ki sequre = 0,50, DF= 2, P = 0,77. Çalışmanız, obez ve obez olmayan kişiler arasında güçlü bir BMI ilişkisi buldu. 30 kişiden 26'sı obez (%86), 30 kişiden 4'ü normal VKİ'ye sahipti (%14). Kreatin takviyesi kullananların serum kreatnin seviyeleri normalden daha yüksekti (p0,01). (633109,11) ve (197,02), normal örneğe göre sırasıyla. idrar kreatnin takviyeli denekler, sağlıklı kontrollerden daha yüksek seviyelere sahipti (P 0,01). Grup 1 ortalama 633109,11 ve Grup 3 197,02 ortalamaya sahipti. 0,001 Kreatin takviyesi olsun veya olmasın, ortalama seviyeler dikkate değerdir (p 0,001). GRUP 1 = 160,5420,67, GRUP 2 = 87,3810,15) ve normal numune (GRUP 3 = 70,1812,91). AST, ALT, ALP, Toplam protein ve albümin, kreatin takviyesi ile değiştirilebilir.

2023, 47 sayfa

Anahtar Kelimeler: Kreatinin temizleme, Kreatin, Vücut geliştiriciler, Kreatinin etkileri, Besin takviyeleri

PREFACE AND ACKNOWLEDGEMENTS

I would like to thank my thesis advisor, Assoc. Prof. Dr. Şevki ADEM, for his patience, guidance and understanding. Finally, I'd like to thank my parents for their unfailing support and encouragement.

Bassam Watheq Abdulateef AL-SHAMMARI
Çankırı-2023

CONTENTS

LIST OF SYMBOLS

mg/dL	Milligrams per decilitre
mL	Milliliter
nm	Nanometer

LIST OF ABBREVIATIONS

A	Absorbance
ADMA	Asymmetric dimethylarginine
ANOVA	Analysis of Variance
BMI	Body Mas Index
CR	Creatnine
CR-CL	Creatnine Crealnce
CrP	Creatine Phosphate
EIZA	Enzyme Immunoassay
K+	Potasium
Na+	Sodium

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1. INTRODUCTION

Some sports necessitate the use of creatine (Cr) in order for the muscles to function properly. The amount of extracellular creatine and the expression and activity of the creatine transporter Creatine proteins were discovered to be the most important determinants of Creatine absorption by researchers. Here, we take a quick look at the variables that affect Creatine protein activity and expression. Exercise and training and Cr co-ingestion with carbohydrate are two methods we're investigating to help boost skeletal muscle Creatine absorption (Morton *et al.* 2009).

The mechanisms by which these variables increase the transit of muscle Creatine are described whenever this is possible. Fiber type and gender influence the skeletal muscle of the human body A study is being conducted on creatine intake and storag (Romeiro *et al.* 2015).

Creatine is mostly metabolized by the pancreas and liver from non-essential nutrients such as arginine, S-adenosylmethionine, and glycine. Creatine is often present in animal products such as meat, fish, and poultry. Approximately 1.6 percent of the creatine in our bodies is broken down each day by the human body. Creatine must be produced or ingested every day to maintain the body's supply. Endogenous production and an omnivorous mixed diet meet about half of this need. The depletion of the Creatine pool is caused by the unregulated, nonenzymatic conversion of creatine and creatine phosphate (CrP) to creatinine. The heart, brain, and testicles all contain trace amounts of creatine, although the majority of it is found in skeletal muscle. As a means of delivering Creatine, which is produced in the liver and pancreas, to the tissues that need it, circulation is employed (e.g., skeletal muscle, brain, and heart (Artioli *et al.* 2019).

More than 90% of the cell's Creatine absorption against a high concentration gradient is due to a Na+ and Cl-dependent Creatine protein (Snow and Murphy 2001).

1.1 Objectives of Study

In this project will be to often use a creatine test to determine the effectiveness of the kidneys, since high levels of the latter in the blood and urine indicate a problem with the kidney with body buliding persons.

1.1.1 Specific

- To determination creatine levels is to treat the cause of their high levels, and there are also many lifestyle and diet changes that you can adopt to contribute to this.
- To evalute creatine levels may rise as a result of excessive protein consumption or high-intensity exercise.

2. LITERATURE REVIEW

2.1 Creatine

In Type II muscle fibers, nitrogen-containing substance creatine is abundant. The brain, liver, kidneys, and testes make up around 5 percent of the body's creatine storage, whereas the remaining 5 percent is present in these four organs together (Figure 2.1) (Mihic 2018).

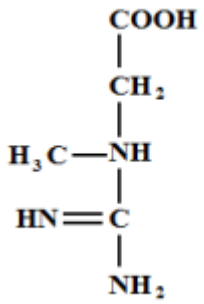

Figure 2.1 Molecular structure of creatine (Mihic 2018)

Muscle building supplement creatine has been a popular choice since it was introduced in the early 1990s. In 2011, 14 million creatine supplements were purchased in the United States. As of 2013, (Eudy 2013). Contrary to popular belief, supplementing with creatine can help people of all ages gain muscle mass, not just those who are young and active. Numerous research have revealed this to be true (Brosnan *et al.* 2016).

2.2 Ergogenic Action

Muscle PCr levels may be increased by taking creatine, which raises muscle PCr concentrations Skeletal muscle contractions are strong and high-intensity because PCr stores allow for rapid ATP resynthesis. To restore ATP stores inside "microdomains," heart and skeletal muscle and brain activity are also essential (Figure 2.2). In cardiac

and skeletal muscle cells, as well as in the plasma membranes of brain cells, CK breaks down PCr and combines it with ADP to produce the ATP needed for muscle contraction. CK is found in these "microdomains," or cellular compartments, where it cleaves PCr and combines it with ADP to produce ATP (Valencia *et al.* 2021).

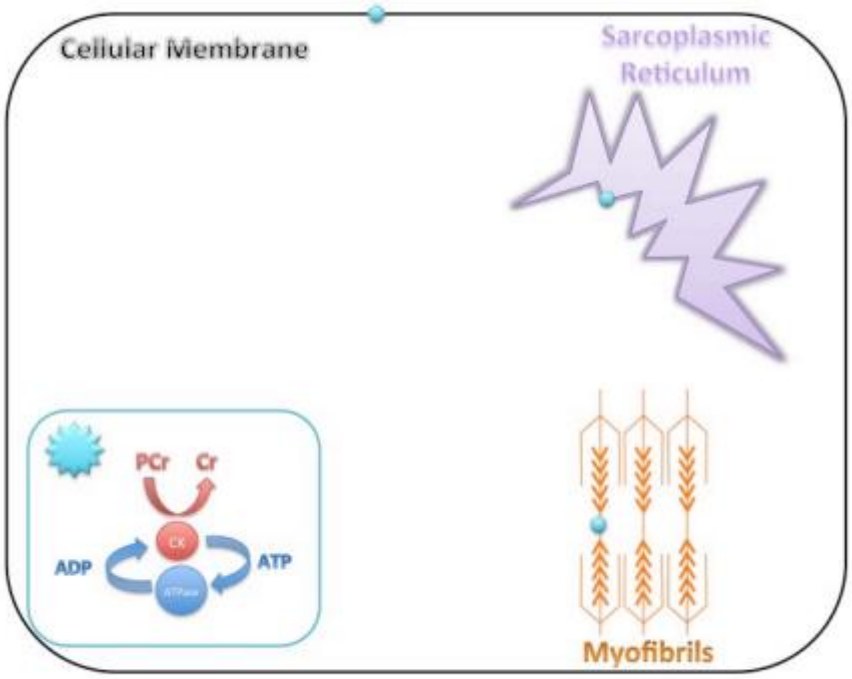

Figure 2.2 Microdomain representation of ATP production (Valencia *et al.* 2021)

Human reproductive tissues contain high-energy phosphagens, which aid cells in maintaining a consistent source of cellular energy. Creatine kinase is the only phosphagen system in higher vertebrates, unlike invertebrates. Finally, the creatine kinase circuit functions as a short-term energy buffer, keeping the cellular ATP turnover and ATP/ADP ratio constant. As shown in (Figure 2.3), the flow of high-energy phosphates (from oxidative phosphorylation and glycolysis, respectively) from ATP-generating sites (such as the mitochondria) to ATP-consuming sites (such as the cytosol) takes place (Kolodiazhnyi 2021).

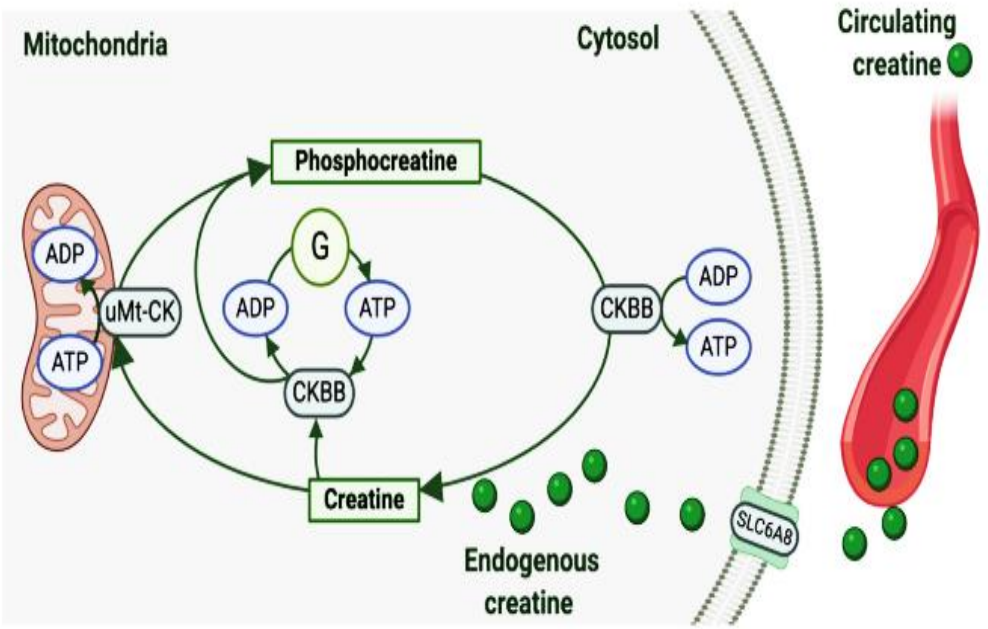

Figure 2.3 The Creatnin loop. Some cells create their own creatine, whereas others get it from the blood (SLC6A8) (Kolodiazhnyi 2021)

This is followed by ubiquitous mitochondrial creatine kinase phosphorylating ATP to creatine, ADP (uMt-CK). The brain-type creatine kinase CKBB produces phosphocreatine and ADP from glycolytic ATP. CKBB then hydrolyzes the connection between creatine and the phosphate group stored as phosphocreatine, releasing ATP and creatine (Kolodiazhnyi 2021).

2.3 Creatine Metabolism

It is possible to buy or make your own creatine. When it comes to the two-step process of creatine generation, GATM alias AGAT and N-methyltransferase are involved. The diagram presented in (Figure 2.4) may be simplified even more (GAMT). Creatine is transported across cell membranes via the sodium and chloride-dependent creatine transporter 1 (CT1, encoded by the gene solute carrier family 6, member 8 (SLC6A8)). As well as the mitochondrial enzymes that are involved in the process of phosphorylating and dephosphorylating creatine (the so-called "CKs") in the brain and the muscles (CKMT). While CKB and CKM directly phosphorylate creatine in the

mitochondria, CKMT phosphorylates creatine in the cytoplasm of the cell. Intellectual disability, developmental delay, and epilepsy are all possible outcomes for people with cerebral creatine deficiency syndrome (CCDS), a condition characterized by a lack of one of the enzymes in the creatine cycle (Leuzzi *et al.* 2013).

Scientists have paid scant attention to fish creatine systems, which have been overlooked. Compared to mammalian muscles, fish muscles have higher creatine concentrations. This suggests a role for creatine. Rainbow trout's endurance was increased by supplementing their meals with creatine in a fixed-speed test As in humans, GATM, GAMT, and CT1 can be discovered in zebrafish. According to a statement made by (Leuzzi *et al.* 2013).

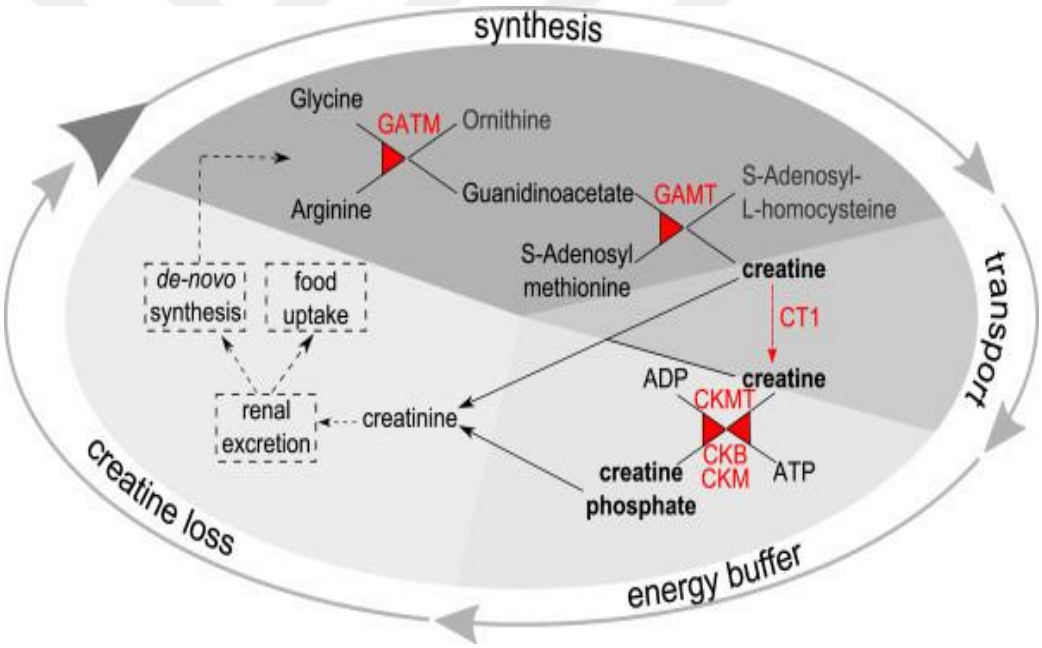

Figure 2.4 A visual representation of the creatine biosynthesis route (Leuzzi *et al.* 2013)

Creatine is synthesized in two stages (Wyss and Kaddurah-Daouk 2000). The first step is to convert glycine and arginase to guanidinoacetate and ornithine. Creatine is made from guanidinoacetate by the enzyme GAMT. For example, the enzymes CKM, CKM2, and CKMT employ phosphate groups on molecules of ADP to phosphorylate creatine molecules, which results in the body's production of creatine phosphate. The reversible

reaction of phosphorylating ADP with creatine phosphate is possible. A protein called creatine transporter 1 (CT1) is responsible for moving creatine across cell membranes. It is necessary to create or absorb creatine every day since creatinine is excreted from the body at a rate of about 2% of total creatine every day.

2.4 Creatine and Aging

Muscle mass and strength decline with age (Rawson *et al.* 2011). The high-energy phosphate metabolism may be to blame for this drop. PCr is mostly found in skeletal muscle, and as muscle mass declines with age, it is reasonable to predict that PCr concentrations would drop as well.

Creatine supplementation has been shown to increase muscular growth and strength in young adults as well as the elderly (Gualano *et al.* 2012).

In other studies, supplementing with creatine had no effect on the health of elderly people. Because of the way creatine is stored, some studies of elderly people supplementing with creatine have revealed no notable advantages. Structural muscle holds the bulk of PCr, with Type II muscular fibers dominating Type I (Candow *et al.* 2015).

There are two reasons why creatine supplementation may have a lower impact on muscle growth and performance in older individuals: muscle mass declines with age and Type II to Type I fibers shift, with Type II fibers displaying preferential atrophy This is supported by research that shows that young adults who take creatine supplements have significantly higher muscular PCr levels than their elder counterparts (Cooper *et al.* 2012).

Pre-existing PCr levels have a key role in Cr supplementation results, and older folks tend to see greater benefits than younger adults in some cases (REF). The effects of

creatine supplementation on the elderly should be studied in greater detail (Cooper *et al.* 2012).

2.4.1 Effect of creatnine with body function

Two individuals with impaired kidney function (interstitial nephritis and focal glomerular sclerosis) improved after ceasing creatine treatment (Tarnipolsky 2010) has cast doubt on both of these studies and claims that patients' reduced renal function was caused by other medications they were taking at the time of the research (cyclosporine and non-steroidal anti-inflammatory drugs). No detrimental effects on the liver or kidneys have been established by creatine supplementation trials, however notable they may be (Tarnopolsky, 2010). No indication of hepatic or renal impairment was identified with long-term use of creatine (30g/day) for up to five years (Tarnopolsky 2010).

Short-term creatine supplementation has been shown to have no impact on endurance performance. Muscle citrate synthase activity increased in both trained and untrained rats after a 4-week period of creatine treatment, according to Brannon et al. A marker enzyme for mitochondrial capacity, skeletal muscle substrate use, and endurance performance during submaximal exercise while creatine supplementation was sustained was citrate synthase. Chronic creatine treatment has been shown to increase muscle GLUT4 expression, which could have an impact on substrate transport proteins and oxidative enzymes (Pitkin 2014).

An rise in body mass was observed following short-term injections of creatine It is common for creatine loading to result in an increase in body mass of between 1.0 and 2.2 kg. Water retention in skeletal muscle is thought to be responsible for this increase in body mass . Other studies have linked increased myofibril protein synthesis and decreased breakdown to creatine consumption . The degree to which creatine loading results in a long-term increase in body mass and fat-free mass is unknown (Close *et al.* 2016).

Creatine supplementation is a well-researched ergogenic assistance for athletes. Muscle growth and athletic performance are enhanced by creatine's ability to boost anaerobic energy capacity and reduce protein breakdown . In addition to its well-known benefits for athletes, creatine can also be used clinically and therapeutically to support already-established medical treatments (Jagim *et al.* 2018).

Research on the therapeutic potential of creatine supplementation has focused on diabetes sarcopenia, osteoporosis, and cancer, as well as rehabilitation, cognition,and cardiovascular health. Creatine is becoming increasingly popular as an adjuvant intervention to help manage disease and/or support recovery following this research as a nutritional strategy to help preserve and improve functional and mental abilities as we age, minimize the risk of chronic disease or support recovery after this research. This special issue's goal is to give in-depth assessments of creatine's involvement in health and disease. Aiming to achieve this goal, we've solicited the contributions from a number of leading creatine experts, and we've urged colleagues to contribute meta-analyses and original studies (Kreider *et al.* 2021).

2.4.2 Effect of creatnine on body mucle strengeth

Muscle mass, strength, and functionality decline as we age. Sarcopenia is a disease that affects both sexes. Sarcopenia can be caused by a lack of exercise, inflammation, and a poor diet Our health and well-being may suffer if we grow older with a weaker body. Sarcopenia increases with age, necessitating the usage of creatine supplements during weight training to counteract this. Muscular growth and isometric muscle strength in senior people (>65 years old) were increased by a 14-week creatine supplementation and intense resistance training regimen. Resistance exercise under medical supervision and supplementation with creatine (three times a week for 12 weeks) elderly adults (60–84 years old) with increased lean tissue mass, lower body strength and endurance, and isokinetic knee flexion/extension power. Candow et al. observed that older men's muscular growth and strength increased, as well as their capacity to sustain bone resorption markers, when they supplemented with creatine and protein. After one year

of resistance training with creatine, postmenopausal women's strength and bone density increased (Forbes *et al.* 2018).

Muscle mass was raised by supplementing with creatine and strength training in older women, while creatine supplementation alone boosted lean mass, according to Gualano and coworkers. With creatine supplementation, both overweight and underweight women's muscle mass was increased (Gualano *et al.* 2014).

A stringent diet is required to lose weight due to the rise in adult-onset obesity as people become older. With age comes a decline in physical ability, which can be dangerous. Adding creatine to a low-calorie diet aids muscle preservation, boosts fat reduction, and lowers adult obesity risk. It is possible to lose weight while preserving muscle mass by taking creatine supplements. Adolescent obesity can be prevented or treated. It may be possible to maintain or increase bone density and muscle mass in the elderly by creatine supplementation and strength training. Although this conclusion appears to be based on existing information, it is possible. Creatine supplementation may aid in weight loss, muscle preservation, and the prevention of adult obesity when used in conjunction with a calorie-restricted diet and regular exercise (Aguiar *et al.* 2013).

2.4.3 Effect of creatnine on cognitive function

Elderly adults and those with modest cognitive impairment have been investigated for their memory and executive function. The anecdotal data points to an improvement in executive function, memory and learning as a result of creatine ingestion. Watanabe et al 2002 found that giving volunteers who were doing repetitive math tasks 8 mg of creatine per day for five days increased brain oxygen consumption and decreased mental weariness. Creatine supplementation at a dose of 5 grams per day for six weeks improved working memory and processing speed. In sleep-deprived volunteers, creatine (20 g/day for 7 days) improved random movement generation and decision-making speed, as well as mental state and balance. They performed better on random number generation, spatial memory, and long-term recollection tests when they took creatine supplements. According to, taking creatine ethyl ester for 15 days increased cognitive

function (Ling *et al.* 2009) Pre-match creatine supplementation increased physical endurance and cognitive performance in a simulated soccer match by seven days. When it comes to aging, creatine supplementation appears to boost brain creatine concentration and/or cognitive function.

2.4.4 Effect of creatnine on glucose control and DM

Effects of glucose and insulin What happens to creatine when it's taken up by the body? When atrophy is reversed, creatine supplementation protects the GLUT-4 transporter deficit . Creatine absorption and muscle glycogen levels can be boosted by carbohydrate and protein intake . As a result, scientists have studied how the body regulates glucose . For 12 weeks, take 5 g of creatine every day was studied by (Gualano *et al.* 2011) in type 2 diabetic patients to see how it affected their ability to exercise. Researchers found that supplementing with creatine improved glucose tolerance after meals, boosted GLUT-4 translocation, and lowered HbA1c (Gualano *et al.* 2011).

When it comes to type 2 diabetes, supplementation might have an impact on glucose absorption via activating the AMPK signaling pathway. Creatine supplements may help patients who are just beginning an exercise plan control their blood sugar and hemoglobin A1c levels. As a result, supplementing with creatine may help control blood sugar levels (Alves *et al.* 2012).

2.5 Kidney Function

The quantity of creatinine excreted per unit of time (CrCl) may be used to measure renal function (usually in milliliters per minute). GFR can be calculated using the following equation, which requires an examination of serum and urine creatinine (SCr) levels and 24-hour urinary volume. SCr CrCl/UCr CrCl Creatine clearance, which is inversely related to muscle mass, is affected by factors such as age, gender, and body composition (Levin 2005).

Women in particular have a wide range of CrCl because of this. CrCl is lower in the elderly than in young adults, and it is even lower in the physically smaller. CDC recommends men's CrCl levels of between 97 and 137 milliliters per minute, while women's levels should be between 88 and 128 milliliters per minute. The normal ranges of creatinine clearance can differ from institution to institution because of factors such as age, gender, and laboratory techniques. A normal flow rate of 74-125 mL/min was used in this study (Dukas *et al.* 2010).

Increasing creatinine clearance readings, which are a consequence of creatine metabolism, usually suggest an increase in creatine consumption, whether through a high-protein diet or supplementation. this. During and after exercise, an increase in creatinine clearance can be seen as a result of muscle injury that may cause creatine or creatinine to escape into the bloodstream Creatine is excreted in the urine, therefore a high creatinine clearance is unusual and usually not a cause for concern, especially in those who take creatine supplements (Almeida *et al.* 2022).

2.6 Liver Function

When bilirubin, AST, alkaline phosphatase, and AST levels are measured in blood, it is possible to determine how well the liver is functioning. There is no need to be alarmed about low levels of these chemicals in the blood. Elevated concentrations of these compounds can pose a variety of health risks, depending on the molecule in question, the amount of concentration, and the ratio of concentration to other concentrations. If ALT levels in the blood are abnormally high (>10 times the normal range), there may be a problem (Poortmans *et al.* 2000).

There is no difference in the way ALT and AST are raised. This includes conditions that are both acute and chronic.

Hepatitis, bile duct blockages, and cancer are all linked to elevated ALP levels in the bloodstream. Biliary obstruction causes ALP (together with bilirubin) to rise

substantially higher than AST and ALT levels in cases of hepatitis. In Paget's disease or bone-metastasizing malignancies, increased bone cell activity can lead to elevated ALP levels. All of the following conditions can generate a moderately elevated ALP level in some people: A variety of bacterial illnesses, including congestive heart failure, ulcerative colitis, and Crohn's disease. Other liver function markers, such as C-reactive protein, must be compared with ALP values in order to rule out liver disease as the root cause. Clinicians can identify if a patient's increased ALP levels originate from the bone or the liver by doing an isoenzyme test (Barcelos *et al.* 2016).

The type of liver dysfunction indicated by an increase in bilirubin varies on the specific form of bilirubin. High amounts of unconjugated (indirect) bilirubin may be due to transfusion reaction, haemolytic anemia, 15 cirrhosis, or increased transfusion reaction. Alcoholism and liver disease (including gallstones and scarring) are all possible explanations for elevated blood bilirubin levels. To determine if a person has elevated levels of conjugated bilirubin in their urine, a dipstick test can be utilized (Barcelos *et al.* 2016).

3. MATERIALS AND METHODS

3.1 Subjects

These findings were obtained through the utilization of study participants at the National Center for GYM ,Baghdad -Iraqi populations. Patients between the ages of 20 and 45 with from peroid ist december 2021 to march 2022.

There are three main divisions:

- Grup A: 40 Sample for normal people.
- Grup B:40 Sample for bodybuilders.
- Grup C 30 A sample of bodybuilders taking nutritional supplements.

The control group consisted of thirty adults ranging in age from 19 to 40, all of whom looked to be volunteers.

3.2 General Information

Each person in this study had to be interviewed in person to get information about their age, body weight , matrial status.

3.2.1 Inclusion criteria

Any budy buliding and normal persons between the ages of 20 and 45 who has been body buliding and agrees to take part in this study is considered a case.

3.2.2 Exclusion criteria

persons with any of the following conditions were not included in this study.

- Diabetes mellitus.
- Immune system disorders, such as lupus.
- Goodpasture's syndrome.
- Gout.
- Rhabdomyolysis.
- muscle atrophy.
- Blood loss due to shock.

3.3 Physical Examination

Using the formula weight in kilograms divided by height in square meters, BMI was calculated for each participant in this study. In order to measure obesity, the WHO's BMI category and the global obesity task force are utilized. By folloing catogries.

- 15 – 19.9 Under weight
- 20 - 24.9 Normal range
- 25.0 – 29.9 Overweight
- >30 obese

3.4 Collection of Blood Sample

To measure the serum concentration, researchers collected 10 mL of venous blood from each participant and centrifuged it at 3000 rpm. The supernatant was then aspirated and kept at - 20 0C until it could be analyzed. Examining the blood serum of both bodybuliding and healthy controls.

- Creatinine clearuce test.
- serum creatnine.
- urine creatnine.
- Total protein , Albumine.
- liver function teset (AST , ALT , BIL , ALP).

3.5 Labrotary Biomarker and Chemicals

Table 3.1 provides a list of the chemicals and devices that were utilized throughout the research.

Table 3.1 Chemicals used in this study

No.	parameters and chemicals	Company
1	Total protein by colometreic method	Germany / Roche/Hitachi cobas c
2	Albumine by colometreic method	Germany / Roche/Hitachi cobas c
3	Creatnine colometreic method	Creatinine – COBAS C311
4	AST colometreic method	Spain biosystem
5	ALT	Spain biosystem
6	ALP	Spain biosystem
7	BIL	Spain biosystem
8	URINE CREATININE	SEMENIZE (URINE ANALYZER)

3.5.1 Determination of TOTAL protein by copus

Total protein in human blood and plasma may be quantified using Roche/Hitachi cobas c devices in vitro. University of Minnesota Advanced Research and Diagnostic Laboratory 1200 Washington Ave S, Suite 175 Minneapolis, MN 55415 (ARDL).

Princible: Perform the test using colorimetry. The pink-to-purple biuret complex is formed when divalent copper combines with protein peptide links in alkaline conditions. Copper hydroxide precipitation and autoreduction are both hampered by potassium iodide and sodium potassium tartrate, respectively. The darker the color, the higher the protein concentration. Absorption at 552 nm is used for photometric measurements.

Expected values:

- 0 – 1 day 4.6 – 7.0 g/dL
- 1 – 7 days 4.4 – 7.6 g/dL
- 7 days - 1 year 5.1 – 7.3 g/dL

- 1 – 2 years 5.6 – 7.5 g/dL
- 18 years 6.0 – 8.0 g/dL
- Adults (ambulatory) 6.4 – 8.3 g/dL

3.5.2 Determination of albumin by cobus

Lab-4215 uses a Roche/Hitachi cobas c system to conduct an in vitro measurement of albumin concentrations in human serum and plasma.

Principle: The test should be carried out using colorimetry. Blue-green complexes of albumin may be formed using anionic dye bromcresol green (BCG), which can be formed with an acidic pH (4.1). In this sample, the degree of blue-green coloration is exactly proportional to the quantity of albumin present.

Expected Values:

Adult: 3.4 – 4.8 g/dL

Pediatric:

- 0-4 days 2.8 – 4.4 g/dL
- 4 days-14 years 3.8 – 5.4 g/dL
- 14-18 years 3.2 – 4.5 g/dL

3.5.3 Determination of creatnine by coubs

Determination of creatnine by Creatinine – COBAS C311, Lab-8814.

Principle: Creatinine levels can be quantified with COBAS Creatinine on Roche/Hitachi Cobas c systems, which is an in vitro assay. By using creatininase and sarcosine

oxidase, this enzyme-based technique converts creatinine into glycine, formaldehyde and hydrogen peroxide. Peroxidase catalyzes the formation of a quinone imine chromogen from the hydrogen peroxide generated during the reaction with 4-aminophenazone and HTIBa. The color intensity of the resulting quinone imine chromogen is influenced by the quantity of creatinine in the reaction mix.

Expected Ranges:

Serum/Plasma:

- Adult Females 0.6 – 1.1 mg/dL
- Adult Males 0.7 – 1.3 mg/dL
- 0 – 4 days 0.3 – 1.0 mg/dL
- 4 days – 2 years 0.2 – 0.4 mg/dL
- 2 - 12 years 0.3 – 0.7 mg/dL
- 12 – 16 years 0.5 – 1.0 mg/dL

3.6 Determination of Urine Creatnine

Assay of Urine Creatinine by Enzymatic Roche Cobas 6000 Analyzer.

Princible: By using creatine and creatinine phosphate, muscles generate creatinine. It is then removed by glomerular filtration in healthy kidneys. Blood and urine are both sources of creatinine. Detection and treatment of renal diseases, as well as monitoring of renal dialysis, can be monitored by creatinine measurement (e.g. total protein, microalbumin). During this enzymatic process, creatinase converts creatinine into creatine. The enzyme creatinase then breaks down creatine into sarcosine and urea. Color products with a wavelength of 546 nm and 700 nm are formed when hydrogen peroxide mixes with the chromophores in the presence of sarcosine oxidase, which turns sarcosine into hydrogen peroxide and glycine. In comparison to Jaffe picric acid-based systems, which are susceptible to interference from non-creatinine chromogens in the

endpoint reaction, this method has an advantage. Refreance range : 1.10-516 mg/dL (urine).

3.7 Determination of Creatnine Clearance

When your muscles are often injured, your body produces creatine as a waste product. The kidneys remove nearly all of it from your blood in the form of urine.

The rate at which the kidneys remove creatinine from the blood is known as the creatinine clearance. Women's creatinine clearance is about 95 mL lower than men's. The kidneys of the person eliminate creatine from 95 to 120 mL of blood each minute. Each of these three factors affects GFR in a unique way. It is possible to measure glomerular filtration rate using creatinine clearance (GFR).

How to Prepare for a Creatinine Glucose Test.

Take creatine for bodybuilding before the creatinine test. Findings from this study show that creatinine levels have risen.

Creatinine testing can be used to evaluate renal function in two ways:

The evaluation of the bladder's ability to produce urine A 24-hour urine sample can be taken and the creatinine concentration measured. This method uses a plastic jar to hold all of your pee for a day before testing it. If you're concerned about a possible kidney problem, this test may be necessary. A single measurement of creatinine and an appropriate calculation can be used to perform tests on the blood glomerular filtration rate. Many computations take into account a person's age, gender, weight, and ethnicity. GFR and creatinine clearance both decrease when blood creatinine levels rise.

CrCl can be produced by combining creatinine levels in blood and urine (from a 24-hour urine sample). The formula for calculating CrCl is as follows Equation 3.1:

$$\text{Creatinine clearance} = \frac{\text{Urine Creatinine}}{\text{Serum Creatinine}} \times \frac{\text{Urine volume}}{\text{Time}} \quad (3.1)$$

3.8 Demination of Liver Function

3.8.1 Analysis of alanine aminotransferase activity

Principle: The pyruvate hydrazone produced with 2, 4-dintrophenyl-hydrazine Equation 3.2 is used to test alanine aminotransferase activity.

$$\text{L} - \text{Alanine} + \alpha - \text{oxoglutarate} \xrightarrow{ALT} \text{pyruvate} + \text{L} - \text{Glutamate} \quad (3.2)$$

3.8.2 Aspartate aminotransferase concentrations were measured

Principle: Equation 3.3 uses 2,4-dintrophenyl-hydrazine Equation 3.3 to create oxaloacetate hydrazone, which is used to assess aspartate aminotransferase.

$$\text{L} - \text{aspartate} + \alpha - \text{oxoglutarate} \xrightarrow{AST} oxaloacetate + L - glutamate \quad (3.3)$$

3.8.3 Testing for the presence of alkaline phosphatase

Principle: Colorimetric methods were used to measure alkaline phosphatase, and the reaction scheme is as follows: Equation 3.4:

$$\text{Phenyl phosphate} \xrightarrow[\text{pH10}]{\text{ALP}} \text{Phenol} + \text{Phosphate} \quad (3.4)$$

Free phenol reacts with 4-amino-antipyrine in the presence of alkaline potassium ferrocyanide to generate a red-colored complex whose absorbance at 510 nm is exactly proportional to the specimen's ALP activity. In order to inhibit increased enzyme activity, sodium arsenate is added to the reagent.

3.8.4 Analysis of bilirubin levels

Principle: Following the diazotization of sulfanilic acid, bilirubin is photometrically evaluated. Only the first of two bilirubin fractions in serum, the glucuronide-bound form of bilirubin, reacts promptly to an accelerator when free bilirubin is dislodged from protein. Total bilirubin (with accelerator) and direct bilirubin are subtracted to arrive at indirect bilirubin (without accelerator). An accelerator or solubilizer can be used as an accelerator or solubilizer to speed up or slow down the rate at which bilirubin is broken down; however, these terms are simply approximations.

3.9 Statistical Analysis

This study used a range of statistical analysis of significances to assess the significance of difference.

Analytical methods such as t-tests were employed to establish the statistical significance of differences between more than two groups. As opposed to percentages, different results were calculated.

For a study to be considered statistically significant, P values of P0.05, 0.01, and 0.001 must be observed.

4. RESULTS AND DISCUSSION

4.1 Demographics and Clinical Characteristics

The clinical characteristic and demographics of person who taken creatini in IRQI gym are presented in Table 4.1 thirty person who body bulder with taking nutretional supplement espicially creatnin supplement were investigated., there were 19 out of 30 (63%) person with age group <35 years and 11 out of 30 (37%) person with age group >35 years Figure 4.1. The age less than 35 is more frequent for nutrtion supplemnt in budy builder . also in our study shown no significant in mean and SD for age in three groups of present study (group 1=29.34±3.76 , group 2= 28.44±4.19 , group3 = 31.17±2.56 ,) Chi sequre = 0.50 , DF= 2 , P= 0.77.

Our project shown the BMI hav a significant correlation between obese group with normal person 26 person out of 30 were obese (86 %) , wherase reminder 4 from 30 have a normal BMI (14%) respictively. As shown in Figure 4.2. When talking about mean and SD theres a significant correlation as compared between BMI in three main group (Chi sequre = 4.50 , DF= 2 , P= 0.033).

Table 4.1 Clinical frequencey of aging and BMI in present study groups

Clinical characterstic	Sub group	bodybuilders taking nutritional supplements	bodybuilders without taking nutritional supplements	Normal sample
AGE	<35	19 (63%)	23 (57%)	22 (55%)
	>35	11 (37%)	17 (43%)	18 (45%)
	TOTAL	30 (100%)	40 (100%)	40 (100%)
	MEAN±SD	29.34±3.76	28.44±4.19	31.17±2.56
	Chi sequre = 0.50 , DF= 2 , P= 0.77			
BMI	NORMAL	4 (14%)	18 (45%)	33 (82%)
	OBESE	26 (86%)	22 (55%)	7 (18%)
	TOTAL	30 (100 %)	40 (100%	40 (100%)
	MEAN±SD	31.2±2.6	26.8±3.55	21.56±72
	Chi sequre = 4.50 , DF= 2 , P= 0.033			

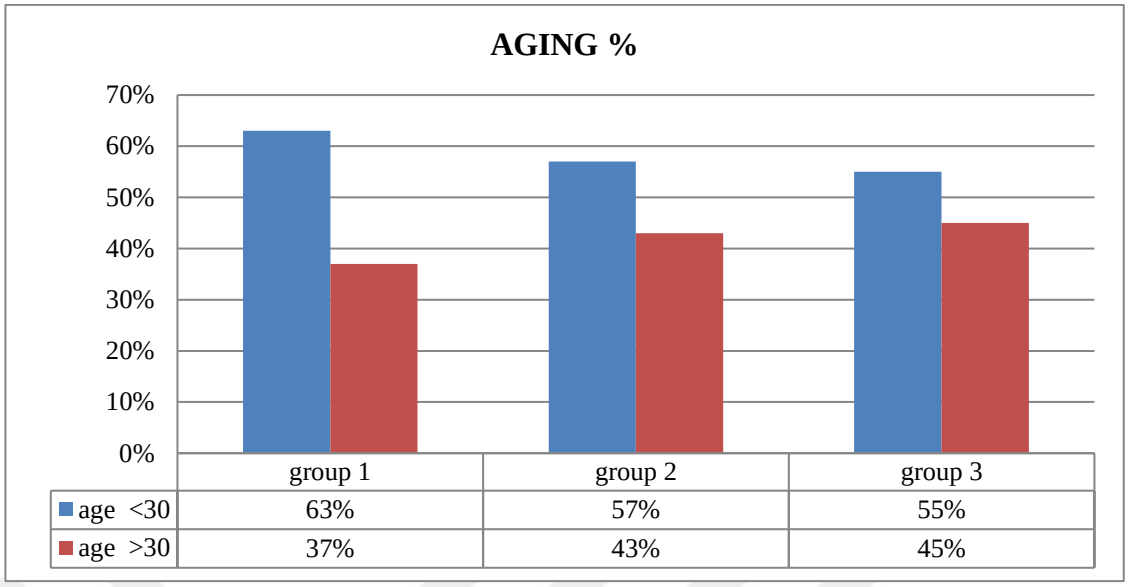

Figure 4.1 Frequencey of age in stedied groups

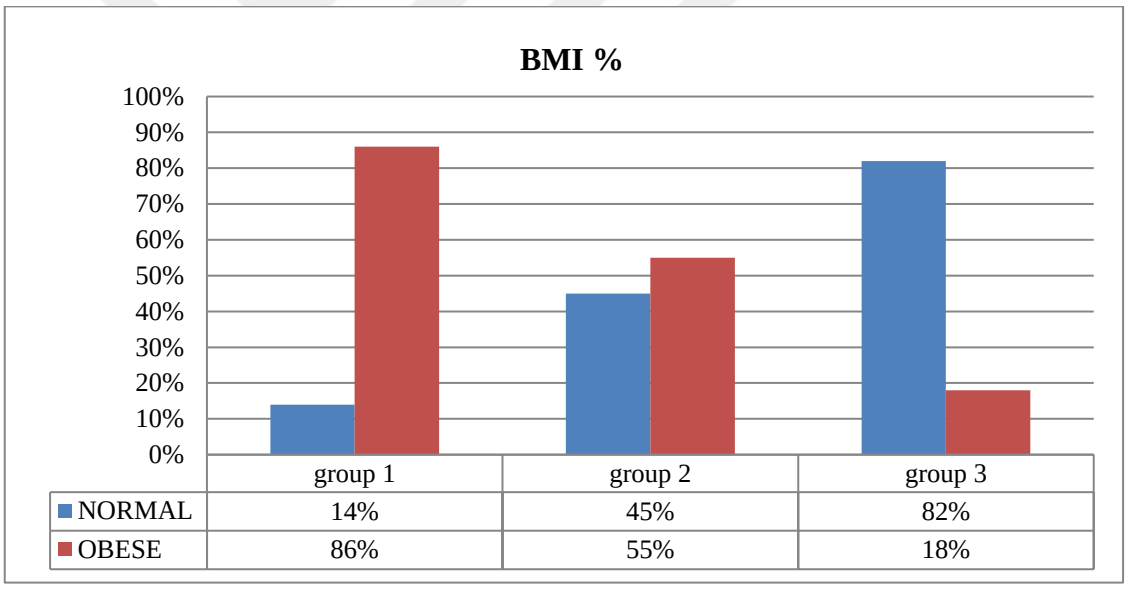

Figure 4.2 Frequencey of BMI in stedied groups

Although creatine supplementation has been proven to boost LBM measurements, the results of individual research tend to be very inconsistent. Thus, the purpose of this research was to conduct a meta-analysis of randomized controlled trials (RCTs) examining the effects of creatine supplementation on lean body mass. Subanalyses were conducted by age group, gender, and exercise modality. Our search of PubMed, SPORTDiscus, the Web of Science, and Scopus followed PRISMA's recommendations

and will remain active until May 2022 (PROSPERO registration number: CRD42020207122). Included were randomized controlled trials that looked at the effects of creatine on lean body mass. Excluded were studies conducted on animals and those conducted on people diagnosed with a certain condition. Eleven hundred and ninety-two people from 35 studies were included. Creatine was shown to improve lean body mass by 0.68 kg (95% confidence interval [CI], 0.26-1.11) when all trials were combined. Subanalyses showed that regardless of age, increases in lean body mass (LBM) were larger when creatine was used in conjunction with weight exercise (MD, 1.10 kg; 95% CI, 0.56-1.65). Creatine supplementation had no significant impact on lean body mass (MD, 0.74 kg; 95% CI, -3.89 to 5.36) or in the absence of exercise (MD, 0.03 kg; 95% CI, -0.65 to 0.70). Additional subanalyses showed that men who took creatine gained 1.46 kg (95% CI, 0.47-2.46) in lean body mass, whereas females gained 0.29 kg (95% CI, -0.43 to 1.01). Overall, creatine supplementation during resistance exercise increases lean body mass. The effects of creatine on men during resistance training are more pronounced than those on females (Delpino *et al.* 2022).

4.2 Creatnine Panale in Stedied Groups

Serum creatnin is indicated in Table 4.2 and Figure 4.3 in this study creatnin was found to be significantly greater in persons who taken creatnine suplement when compared to normal sample ($p < 0.01$). (mean 1.72± 0.4, 0.89±0. 31) are the mean values with control sample . p value 0.001

Table 4.2 and Figure 4.4 show the urin creatnine for persons with creatnine suplement was significantly increased when compared to that of healthy controls ($P < 0.01$). Both group 1 and group 3 had an average value of (633±109.11 and 19±7.02). P- value 0.001

Mean of creatnine clerance levels in creatnine suplment and healthy controls are shown in Table 4.2 and Figure 4.5. In compared to healthy controls, body building with and without creatnine supplement, mean levels have significant ($p < 0.001$). There mean and SD (GROUP 1= 160.54±20.67, group2 = 87.38±10.15) as compared with normal sample (group 3 = 70.18±12.91).

Table 4.2 Mean andSD of creatnin c in stedied clerance group

Creatnine panale	Group 1	Group 2	Group 3	p-value		
				1x2	1x3	2x3
Serum creatnine	1.72± 0.4	1.4± 1.22	0.89±0. 31	0.03	0.001**	0.001*
Urin creatnine	633±109.11	322±77.53	19±7.02	0.01	0.001**	0.001**
Creatnine clerance	160.54±20.67	87.38±10.15	70.18±12.91	0.001	0.001	0.050

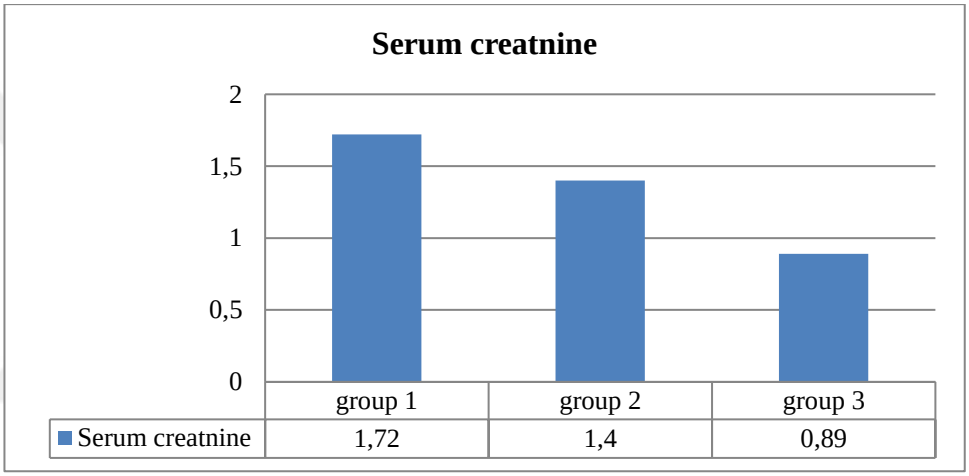

Figure 4.3 Mean and SD of serum creatnine in stedeied groups.

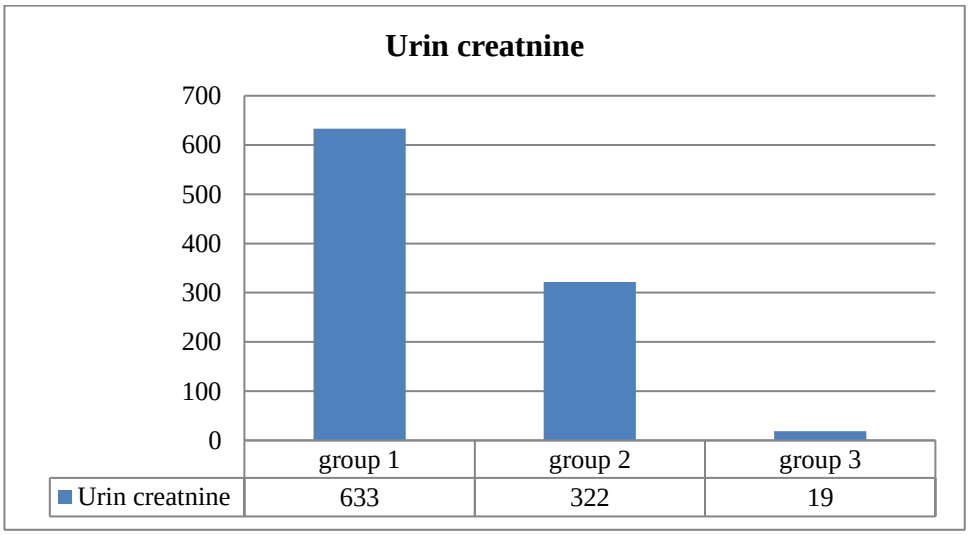

Figure 4.4 Mean and SD of urin creatnine in stedeied groups

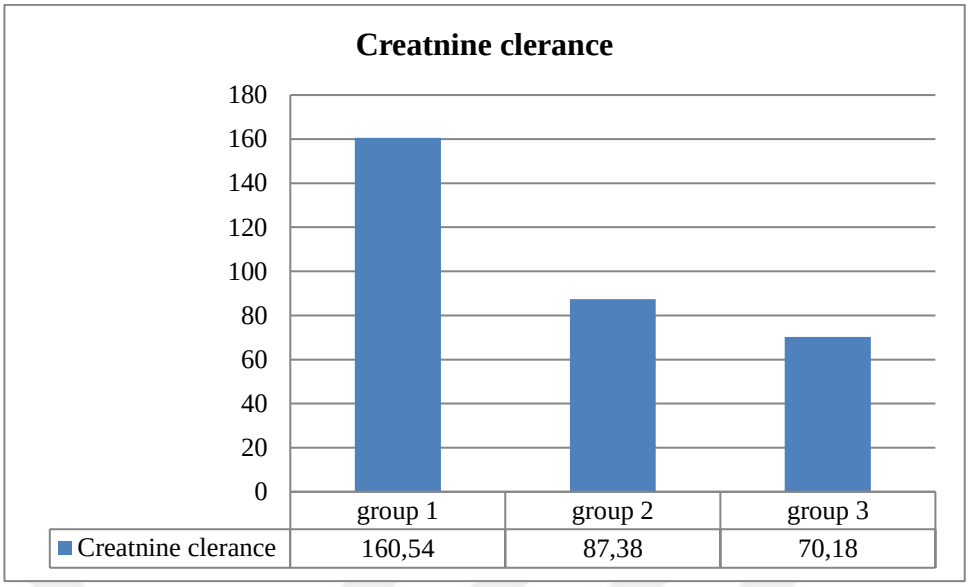

Figure 4.5 Mean and SD of creatnine clerance in stedeied groups

These results, along with those from studies conducted 30 years earlier, formed the basis for the first articles to examine the effects of creatine on normal renal function. 5-7 Eight years after initially being diagnosed with focal segmental glomerulosclerosis, a 25-year-old man was still experiencing regular relapses in 1998, according to nephrologists. After five years of cyclosporine treatment, his kidney function had returned to near normal and he had stopped producing protein in his urine. As a soccer player, he supplemented with creatine. He started with a loading dose of 5 g of creatine three times per day for seven days, then maintained his supplementation with 2 g per day for another seven weeks. After 7 weeks, creatine caused a 60% decrease in creatinine clearance. His creatinine clearances increased after he stopped taking creatine. This paper in The Lancet raised the first known safety concerns about oral creatine (Greenhaff 1998).

Creatine can be broken down into creatinine in the liver and skeletal muscles without the use of enzymes. For nephrologists, serum creatinine has long been a standby for gauging kidney health. However, some non-kidney-related variables, such as protein consumption and muscle mass, may influence the level. Within two hours of consuming meat, serum creatinine levels may increase by as much as 50 percent and stay elevated for up to 24 hours. When used for less than one month, creatine supplements are

considered temporary. Experiment-based research is the backbone of the scientific method. To investigate the potential negative effects of creatine on renal function in the short term, Edmunds and colleagues performed an experiment. In an animal model of cystic fibrosis, they observed that administering a loading dose of 2.0 g/kg of creatine for one week, followed by a maintenance dose of 0.5 g/kg of creatine for five weeks, sped up the course of the illness (such as blood urea concentration and creatinine clearance) (Edmunds *et al.* 2001).

Medical studies. Any plan that requires less than 20 g of creatine per day is considered a low-dose plan. Clinical studies have shown that short-term creatine treatment has no deleterious impact on renal functions, although the long-term consequences on creatinine levels remain unknown. For 5 days, healthy guys were given 20 grams of creatine each day, Poortmans and Francaux discovered that neither the creatinine levels in the subjects' urine nor their serum changed, nor did the subjects' excretion rate or clearance of the drug. 5 Similarly, a 5-day course of oral creatine (20 g/d) in a placebo-controlled trial including healthy male college students resulted in elevated plasma and urine creatinine concentrations without altering creatinine clearance or albumin excretion rate. 6 Males participating in physical education saw comparable benefits from taking creatine on a regular basis for the same amount of time. Creatine supplementation increased total body mass and free fat mass without changing plasma creatinine or creatinine clearance, which is consistent with the results of a randomized, double-blind, placebo-controlled study done on both sexes in 2000 (Mihic *et al.* 2000).

Despite these results, the outcomes of other clinical trials demonstrated that even brief treatment of creatine could alter either serum creatinine concentration or creatinine clearance. Creatine supplementation at 20 g/d for six days resulted in elevated muscular creatine levels. After continuing to supplement with creatine at the maintenance dosage of 2 g/d for an additional 30 days, the rise in muscle creatine concentration remained. The levels of creatinine in the blood and the urine both went up. 4 Creatine treatment (15.75 g/d) for 28 days increased blood creatinine content, total body weight, fat mass, and bone free mass in a randomized double-blind experiment of football players, supporting these findings. 16 After 5 days and 9 weeks of taking 20 g/d of creatine,

there was a 25% and 40% rise in serum creatinine concentration, respectively (Robinson *et al.* 2000).

The kidney may be damaged by creatine in other ways as well. Creatine can be broken down into sarcosine, which in turn can lead to the formation of methylamine and other potentially toxic byproducts. Methylamine may be converted into formaldehyde with the help of semicarbazide-sensitive amine oxidase, another deadly toxin. 19 Methylamine and formaldehyde are toxic to the kidney, intestinal epithelium, and endothelial cells. 19, 20 After 14 days of supplementing with 21 grams of creatine monohydrate per day, Poortmans and colleagues found that plasma creatine content and creatine urine excretion rate increased by about 141% while plasma creatinine levels and creatinine output remained unchanged in healthy volunteers. It was also shown that the amounts of formaldehyde and methylamine in the urine increased by 9.2 and 4.5 times, respectively, after taking creatine supplements for 24 hours. However, neither urine methylamine nor formaldehyde were significantly linked to plasma creatine (Wyss *et al.* 2000). The effects of taking 20 g/d of creatine on a high vs low schedule for 5 days were studied by Sale and colleagues. Creatine was administered to two groups, one of which got 20 grams daily while the other received 5 grams four times day. Creatine was retained in the body and, most likely, the muscles since the single dosage therapy decreased creatine elimination (Peter *et al.* 2003). By spreading the dose of creatine out evenly throughout the day, we were able to diminish the peak plasma concentration and, in turn, the amount of methylamine discharged in the urine. Last but not least, a randomized, double-blind trial showed that taking 0.3 g/kg/d of creatine for seven days elevated urine formaldehyde levels by 30.4% and by 63.4% in the groups that participated in resistance exercise compared to the groups who did not. This finding indicates that resistance training may substantially reduce the elevation of urine formaldehyde excretion due to creatine consumption (Poortmans *et al.* 2005).

Long-term supplementation with creatine refers to using the substance for a period of months to years. Negative Effects of Chronic Creatine Intake on Kidney Function. The effects of using creatine on a long-term basis are still being investigated. Long-term usage of creatine (21 g/day for 5 days, and 3 g/d for the following 58 days) had no

significant effect on creatinine clearance, urea clearance, or albumin excretion rate in healthy men, according to a randomized, placebo-controlled research. 5 Creatine supplementation for 10 months to 5 years had no effect on the clearance of urea, urine albumin, or creatinine in another trial. I Long-term supplementation with creatine refers to using the substance for a period of months to years. Long-Term Effects of Creatine on Kidney Function. The effects of creatine use over the long term have not been fully explored. Long-term use of creatine (21 g daily for 5 days and 3 g/d for 58 more days), compared to the control group (5 days of 21 g of induction dosage followed by 58 days of no dose at all), had no discernible influence on the pace at which healthy males excreted creatinine, urea, or albumin. There was no change in urine output, urea clearance, urine albumin, or creatinine clearance in another trial when creatine was administered to healthy athletes for 10 months to 5 years. 7 Similarly, Mayhew and colleagues found no long-term adverse effects on kidney function indicators in the American College of Football Players who consumed 5 g/d to 20 g/d of creatine for 0.25 to 5.6 years. 25 Pline and Smith discovered that in young, healthy people, creatine supplementation for up to 5.6 years and acute administration of high doses of creatine for four to five days had negligible effects on creatinine concentrations and renal function. 26 To sum up, the most recent adequate randomized double-blind placebo-controlled investigation demonstrated that high-dose creatine supplementation (about 10 g/d) had no adverse effects on healthy males engaging in aerobic activity.

Besides the randomized and retrospective studies16,29, there is at least one case report that suggests creatine supplementation may cause renal damage. An 18-year-old male presented to the emergency room complaining primarily of nausea, vomiting, and stomach pain, per the report of Taner and coworkers. During 5 days, he took 20 g/d of creatine as a bodybuilder, and for the following 6 weeks, he took 1 g/d. He registered at 150/90 mm Hg. Serum urea (39.98 mmol/L), creatinine (201.55 mmol/L), and uric acid (0.37 mmol/L) were all above normal at admission. A normal range was found for all biochemical and blood-related indicators. Urine testing alone revealed proteinuria, with a 24-hour protein excretion of 284 mg. A kidney biopsy suggested the likelihood of acute tubular necrosis despite normal renal ultrasonography findings. Creatine supplements were stopped and intravenous fluids were given while hospitalized. The

patient's BP, Creatinine, and Proteinuria were all normal after 25 days. 29 High serum creatinine levels and low estimated glomerular filtration rates were only two of the indicators that four instances presented with renal function concerns. They had all been diagnosed with HIV infection and were on a variety of antiretroviral drugs. They used whey protein and creatine to look more muscular. One of them, for no particular reason, took in 24–30 g of whey protein and 5–10 g of creatine monohydrate daily. Eliminating the supplements and keeping a close eye on the patients helped reduce their serum creatinine levels. The researchers concluded that creatine and concentrated protein supplements generated elevated blood creatinine levels and incorrectly calculated glomerular filtration rates, both of which contributed to incorrect diagnosis of renal illness. Human immunodeficiency virus (HIV) patients may be particularly susceptible to these misconceptions either to the virus itself or because of changes in muscle and fat distribution brought on by certain drugs in fit athletes (Willis *et al.* 2010).

Similarly, Mayhew and colleagues found no long-term adverse effects on kidney function indicators in the American College of Football Players who consumed 5 g/d to 20 g/d of creatine for 0.25 to 5.6 years. 25 Pline and Smith discovered that in young, healthy people, creatine supplementation for up to 5.6 years and acute administration of high doses of creatine for four to five days had negligible effects on creatinine concentrations and renal function. 26 Last but not least, the most recent relevant randomized double-blind placebo-controlled study demonstrates that high-dose creatine supplementation (approximately 10 g/d) had no adverse effects on healthy males engaged in aerobic activity (Taner *et al.* 2009).

Besides the randomized and retrospective studies16,29, there is at least one case report that suggests creatine supplementation may cause renal damage. An 18-year-old male was taken to the hospital, mostly due to his complaints of nausea, vomiting, and stomach pain, as reported by Taner and coworkers. During 5 days, he took 20 g/d of creatine as a bodybuilder, and for the following 6 weeks, he took 1 g/d. He registered at 150/90 mm Hg. Serum urea (39.98 mmol/L), creatinine (201.55 mmol/L), and uric acid (0.37 mmol/L) were all above normal at admission. A normal range was found for all biochemical and blood-related indicators. Urine testing alone revealed proteinuria, with

a 24-hour protein excretion of 284 mg. A kidney biopsy suggested the likelihood of acute tubular necrosis despite normal renal ultrasonography findings. Creatine supplements were stopped and intravenous fluids were given while the patient was hospitalized (Sale *et al.* 2009).

After 25 days, the patient's blood pressure, serum creatinine, and proteinuria were all back to normal. 29 Nonetheless, significant blood creatinine levels and low estimated glomerular filtration rates were seen in four of the presented cases, calling the renal function into doubt. All had been diagnosed with HIV and were on various antiretroviral medications. They used whey protein and creatine to look more muscular. One of them, for no particular reason, took in 24–30 g of whey protein and 5–10 g of creatine monohydrate daily. Eliminating the supplements and keeping a close eye on the patients helped reduce their serum creatinine levels. The researchers concluded that creatine and concentrated protein supplements generated elevated blood creatinine levels and incorrectly calculated glomerular filtration rates, both of which contributed to incorrect diagnosis of renal illness. Because of the human immunodeficiency virus or because of changes in muscle and fat distribution brought on by certain drugs, patients with AIDS may be more prone to such errors (Gualano *et al.* 2008).

Creatine's primary cellular environment is striated muscle, where it is phosphorylated to transfer one of its phosphate molecules from ADP to ATP. After being synthesized from creatine, creatinine is flushed out of the body in urine by the kidneys. A small amount of peritubular capillary secretion might cause creatinine, which is freely filtered at the glomerulus, to overestimate its true value when used to determine glomerular filtration. Human creatinine synthesis is mostly constant, albeit it is affected by total body mass, especially muscle, and by the amount of exogenous creatine consumed, usually in the form of animal protein (usually small effect). Creatine supplementation can increase daily dietary consumption from the typical 1 g to the more optimal 25-30 g (Willis *et al.* 2010).

Because creatinine synthesis is rather stable and elimination occurs only in the kidneys, it has been employed as a surrogate measure for renal function because only changes in

intake or elimination, i.e. renal disease, can modify creatinine levels that are easily detectable. There is speculation that creatine supplements may have ergogenic effects, and athletes have been using them for decades. Creatine supplementation has been linked to renal impairment in some publications , however this is still up for debate since many other research have shown that it has no effect on healthy people's kidney function and does not even increase their serum creatinine levels (Gualano *et al.* 2008).

Dietary creatine supplementation has been previously associated to a significant rise in creatinine and apparent renal impairment as evaluated by estimated GFR using the MDRD equation . Creatinine levels in that series, however, increased to a maximum of 166 mol/L due to the usage of creatine supplements by HIV-positive people, while eGFR vacillated between 41 and 60 mL/min/1.73 m2. It was hypothesized that a malnourished person's underlying HIV would make the effect of creatine supplementation on muscle metabolism and, thus, creatinine levels, much more pronounced (Gualano et al. 2008).

Boldenone (Equipoise), a widely used anabolic steroid, increases both cow growth and feed conversion, leading to more efficient meat output. Instances of horse doping have also been linked to it. Bodybuilders like it because it increases appetite and erythropoietin production. The patient's creatinine levels may have increased due to the anabolic steroid-induced muscle growth, but the changes were too dramatic to be explained by that mechanism. As his creatinine clearance was far greater than his GFR had been projected to be, it was determined that the rise in creatinine was not due to a decrease in waste product elimination (Herlitz *et al.* 2010).

An initial diagnostic challenge in this case was the patient's seemingly rapidly increasing creatinine level without a clear history of ingestion of an exogenous drug. Since there was no protein in the urine and the nephritic screen came back negative, a biopsy was deemed unnecessary, but the diagnostic limbo persisted while urine tests were being run. This case illustrates the importance of maintaining a high index of suspicion for alternative causes of higher creatinine levels instead of presuming elimination failure or renal disease is to blame. Diagnosis clues included fluctuating

creatinine levels, with drops during admission when abuse was not possible and a rapid rise after discharge, and the absence of other signs of renal disease (such as elevated urea, elevated phosphate, a normal urinary protein-creatinine ratio, low hemoglobin, etc.) (Herlitz *et al.* 2010).

4.3 Liver Function and in Stedied Groups

The average total protein concentrations in sample with creatnine supplement and healthy controls are shown in Table 4.3 and Figure 4.6. This finding that persons with creatnine mean values were substantially increased than those of healthy controls ($p< 0.05$) in their study. There is a significant difference between the total protein levels of persons with creatnin and without it and those of healthy controls (mean 7.75 ± 0.9 , $6.95 \pm 0.5$and $5.23\pm$ 0.55 mg/dl).

Total serum albumin concentrations in person who taken creatnine supplement and normal sample are shown in Table 4.3. Means ($p <0.01$) for creatnine group and without suplement were slightly significantly higher than those for the control group. The average albumin values in creatnine suplement and without are 5.56 ± 0.26 and 4.70 ± 0.32 , respectively. (mean 4.46 ± 0.26) is the control group mean (mean).

In present study levels of liver function teset in the blood are shown in Table 4.3. According to the results, standard for comparison. $P <0.01$ implies that the mean of creatnine supplement and normal sample are not significantly different.

Table 4.3 Mean and SD of liver function in creatnine suplement and control groups

Liver function	Group 1	Group 2	Group 3	p-value		
				1x2	1x3	2x3
Total protein	7.75 ± 0.9	6.95 ± 0.5	5.23±0.55	0.34	.01	0.015
Albumin	5.56 ± 0.26	4.70 ± 0.32	4.46 ± 0.26	0.01	0.001	0.038
AST	45.18±8.73	33.46± 5.39	19.65± 3.8	0.01	0.01	0.01
ALT	66.836±4.68	48.74± 6.12	22.54± 3.76	0.027	0.001	0.015
ALP	235± 37.78	170± 20.9	100± 19.66	0.001	0.001	0.025
Bilrubin	1.3±0.21	0.9± 0.12	0.57± 0.076	0.028	0.011	0.020

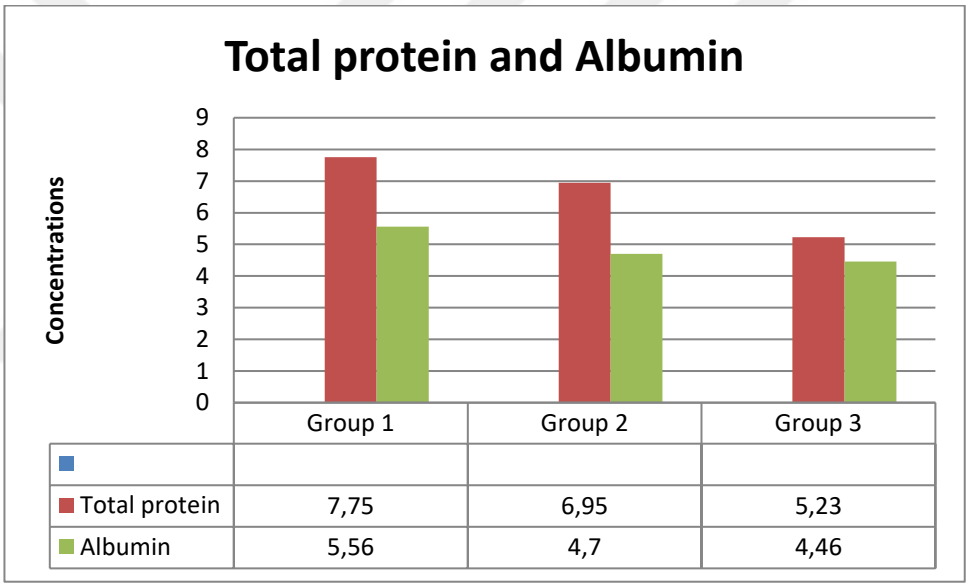

Figure 4.6 Mean and SD of total protein and albumin in stedeied groups

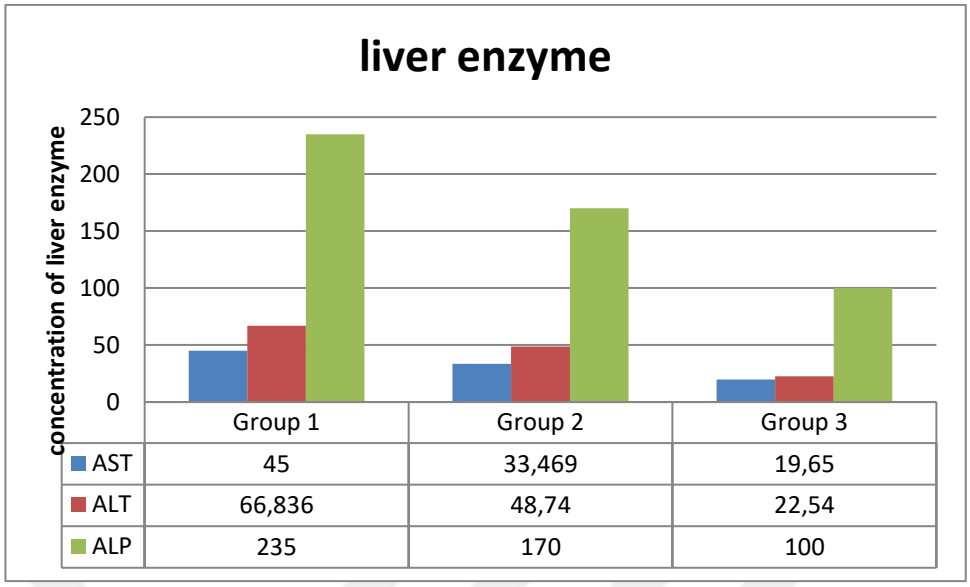

Figure 4.7 Mean and SD of liver enzyme in stedeied groups

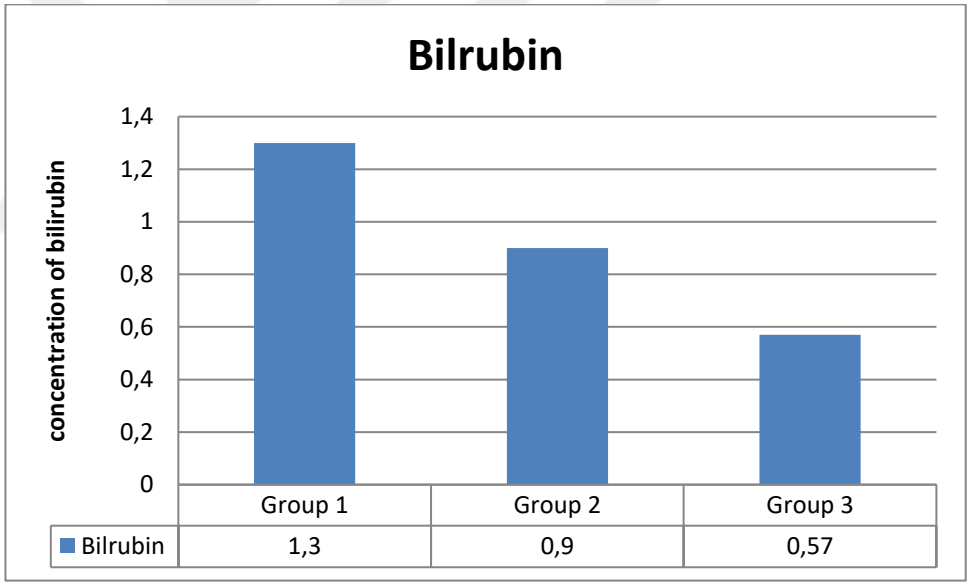

Figure 4.8 Mean and SD of bilirubin in stedeied groups

Furthermore cyclical was his eating pattern. For the first three months, he ate a high-calorie, high-protein diet in an effort to build muscle. Subcutaneous fat was then reduced by a period of calorie restriction. He self-administered the diuretic torasemide and drastically limited his salt and water intake to better define his muscular contour by reducing the amount of extracellular and subcutaneous tissue.

As compared with another stedied the patient began showing symptoms after 6 months of AAS treatment and 1 month of treatment with diuretics and a limited diet. After that, he stopped training and medicating himself, and was eventually brought to our hospital's emergency room. During a month, the patient suffered from asthenia and anorexia. Analytical data reflected acute renal failure (urea: 304 mg/100 ml; creatinin: \s10.2 mg/100 ml), muscular damage (myoglobinuria; CPK: \s5499 IU/l; ALT: 178 IU/l; AST: 130 IU/l; LDH: 716 IU/l), \smetabolic alkalosis (pH: 7.62; Pco2: 66.1 mm Hg; Po2: \s80.6 mm Hg; HCO32: 77.8 mmol/l), hypokaliaemia (K+ \s: \s2.12 mEq/l), and hypernatraemia (Na+ \s: 147 mEq/l). No regular cigarette or alcoholic beverage use was reported. It's common knowledge that AAS contribute to hypernatraemia and fluid retention. An excess of sodium in the blood causes an increased rate of potassium and hydrogen ion excretion, leading to metabolic alkalosis and hypokalemia, a persistent slowing of respiration, and compensatory respiratory acidosis. The bodybuilder's severe hypokalemia may have been caused by his self-administration of a loop diuretic and his failure to maintain an adequate intake of Na+, K+, and water throughout the training sessions (Grazioli *et al.* 2001).

Comparing males and females over all decades of life, (Mera *et al.* 2008) found that females consistently had lower levels of AST and ALT than males, with the exception of the 10th and 11th decades (p 0.05). . Median AST levels were 24 U/L for women and 26 U/L for men. Median ALT levels were 26 U/L in females and 32 U/L in males. The serum levels of AST and ALT were higher in women in their 10th and 11th decades compared to men, although this difference was not statistically significant. 5 Although there was no evidence of liver disease in the patients, the fact that comorbidities, body mass index, and social history were not included casts doubt on the validity of their findings.

Even Nevertheless, Bussler et al.6 found higher levels of AST and ALT in males than in girls, and their investigation was prospective and had a sizable sample size. In contrast to the (Mera *et al.* 2008) Study , the participants in this study were healthy, not on any hepatotoxic drugs, and of a normal body weight. It was shown that ALT levels increased around the time of puberty in both sexes.

In a study of healthy people without a history of liver illness who were hospitalized for experimental purposes2, elevated levels of AST and ALT were found to be 5% and 17.5%, respectively, beyond the upper limit of normal. The restricted hospital diet and lack of exercise were suspected as contributing factors. Hence, diagnosing increased aminotransferases in patients who otherwise seem healthy can be difficult. Intense exercise or the usage of supplements that cause liver and/or muscle damage put bodybuilders at risk for increased aminotransferases (Bussler *et al.* 2018).

4.4 Personal Correlation

Present atudey illustrate a personal correlation between creatnine panale correlation witha nother biochemical marker as shown in Table 4.4.

Table 4.4 Personal correlation of biomarker in syedeid groups

PARAMETERS	CREATNINE (mg/dl)	
Urin creatnine	Correlation	0.567
	Significant value	0.001 **
Creatnine clerance	Correlation	0.490
	Significant value	0.0021**
Total protein	Correlation	0.256
	Significant value	0.18 NS
Albumin	Correlation	0.22
	Significant value	0.101 NS
AST	Correlation	0.30
	Significant value	0.035 *
ALT	Correlation	0.34
	Significant value	0.03*
ALP	Correlation	0.41
	Significant value	0.01*
Bilirumin	Correlation	0.133
	Significant value	0.197

Study participants will include both bodybuilders and non-bodybuilders to see whether powder protein consumption affects blood total protein and creatinine levels. Serum total protein concentrations in all three groups were found to be within the normal range by the spectrophotometer (P 0.01). When comparing groups A and B to group C, the serum creatinine levels were significantly different (P 0.01). The significance level is

0.01. A and B's average results were out of the usual, whereas C's average results were within the permissible range. According to the research, powder protein intake does not have an impact on blood serum total protein concentration. Serum creatinine concentrations are connected to the amount of powder protein ingested. Although blood creatinine levels in groups A and B were found to be too low, group C was found to be consuming an acceptable amount of powdered protein, which ranged from 1.2 to 1.14 grams per kilogram of body weight per day. Group C's serum creatinine levels are both normal and abnormal in groups A and B. When the blood creatinine level drops below normal, patients need to eat enough protein to prevent kidney impairment caused by a lack of protein intake. The kidneys of both trained and non-trained bodybuilders were found to be negatively influenced by long-term low and high protein intake (Omar 2016).

Urine pH was not substantially different between the groups (P 0.01), and protein was not a cause for worry because it occurred under a number of conditions, such as cold exposure, mental stress, heat exposure and physical activity, all of which can cause protein in the urine to build. As a result, renal disease is not indicated by these symptoms Omar 2016).

Bilirubin and liver enzymes – alanine aminotransferase (ALT), alkaline phosphatase (ALP), and aspartate aminotransferase (AST) – are the primary indicators of liver function. No need to worry about these compounds in the blood if they are present at low quantities. Depending on the chemical, the amount of elevation, and the ratio of these compounds to each other, increased levels might suggest a variety of health issues. 14 acute (>10x normal range) elevations in ALT are indicative of a serious condition (Singal *et al.* 2015).

Similar to ALT, AST is high in certain situations. Acute (>10x normal range) and chronic (>10x normal range) are included in this category.

Patients with hepatitis, blockage of the bile ducts, and liver cancer will all have elevated ALP levels in their blood. This means that in hepatitis, the ALP level is considerably

lower than the other two enzymes, but that when the bile ducts are blocked, the ALP level increases significantly (together with the bilirubin). Also, increased bone cell activity may be a sign of Paget's disease or malignancies that have migrated to the bone. Hodgkin's lymphoma, congestive heart failure, ulcerative colitis, and some bacterial infections may all induce moderately elevated ALP. Because of this, ALP readings must be compared to other liver function indicators in order to identify whether the cause is liver-related or symptomatic of a different illness. If the signs and symptoms or other regular tests are unclear, an ALP isoenzyme test may also be conducted to identify whether the elevated ALP is from bone or liver (Kim *et al.* 2013).

The nature of increased bilirubin depends on the kind of bilirubin that is raised, which signals liver impairment. Unconjugated (indirect) bilirubin levels beyond the normal range may be an indication of hemolytic or 15 pernicious anemia, cirrhosis, or a negative response to blood transfusions. There are several reasons why conjugated (direct) bilirubin may be elevated, including viral hepatitis, medication responses and alcoholism, as well as blockages of the bile ducts (such as gall stones or scarring). Bilirubin may be present in the urine if conjugated bilirubin levels are high enough, and a dipstick test as part of a urinalysis may identify it (Barcelos *et al*. 2016).

Fatigue in the periphery may be caused by metabolic waste products and/or the depletion of phosphate reserves during high-intensity activity (Kent-Braun *et al.* 2012) The accumulation of Pi and subsequent decline in the PCr/Pi ratio play a critical role in the development of cancer, according to research.

Increasing intracellular phosphorylation may be a factor in the study's findings, which show an increase in exercise performance. Found a link between exercise performance and the slope of the PCr/Pi ratio following a high-fat or high-carbohydrate diet. A decrease in the PCr/Pi slope and an increase in exercise tolerance may have occurred as a result of this study's creatine loading technique, as Larson et al. state, which is consistent with the findings of this study (Kent-Braun *et al.* 2012).

Muscle tiredness is influenced directly by the accumulation of Pi, and the time it takes to exhaustion is controlled by PCr's involvement. Indirectly, pi build-up can reduce force production by limiting cross-bridge functioning (Kent-Braun *et al.* 2012). Ca2+ processing in the sarcoplasmic reticulum and myofibrillar membrane may potentially influence production in an indirect manner (Kent-Braun *et al.* 2012).

That is why delaying the development of muscle fatigue by altering intracellular phosphorylation potential should help delay the onset of muscle fatigue. Increasing intracellular PCr reserves can reduce the time it takes to exhaustion during high-intensity exercise (Welsch 1996).

5. CONCLUSIONS AND RECOMMENDATION

5.1 Conclusions

- Serum creatnin rises significantly in both types body buliding. And non-probably affect of age in physical activity when taken creatnine suplement.
- BMI hav a significant correlation between obese group with normal person 26 person out of 30 were obese (86 %) , wherase reminder 4 from 30 have a normal BMI (14%) respictively.
- In this study creatnin was found to be significantly greater in persons who taken creatnine suplement when compared to normal sample ($p < 0.01$).
- Present study shown a significant correlation in liver function when compared the creatnine supplement group and normal sample.

5.2 Recommendations

- Examination the relationship between enzymatic, such as creatnine kinase, and trace components in the body buliding.
- Agentic study should be preformed on many protein and enzymes such as CK AND TOTAL PROTEIN in body buliding samples.

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