

## **RHABDOMYOLYSIS: A RARE DISEASE THAT CAN BE PREVENTED**

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**Abstract:** The aim of the study was to identify the relationship between Rhabdomyolysis and its potential severity through early recognition of the diagnosis. Understanding its pathophysiology, being able to identify and diagnose the disease quickly in order to obtain an adequate and effective treatment, reducing metabolic complications and determining possible preventions. This way, data on rhabdomyolysis were collected in the Notifiable Diseases Information System (SINAN), from January 1, 2017 to December 31, 2021, and classified according to the following aspects: hospitalizations by color/ethnicity, sex and character of care in Brazil. The study of this article has a descriptive approach. As for the result from the analysis of hospitalizations according to gender, males had the highest incidence in all years, standing out in 2019 and its lowest number was in 2021. In contrast, females have the lowest number of hospitalizations, the lowest indicator was in the year 2021 and the highest number of hospitalizations was in the year 2019. lower rate in 2021 when compared to the elective scenario, there is a lower demand for medical services. It is seen that in hospitalizations according to color/ethnicity it is portrayed based on the recorded data, the color and ethnicity that most obtained the diagnosis of rhabdomyolysis was the mixed race in 2019 and 2021. Thus, it is concluded that the earlier the diagnosis is made, the more an adequate treatment can be instituted early, however rhabdomyolysis is a disease still little known and rare, so it is of paramount importance more bibliographic studies and case reports that bring an effective and accurate pathophysiology and treatment avoiding the difficult management and systemic damage.

**Keywords:** Rhabdomyolysis, emergency, insufficiency renal

## INTRODUCTION

Rhabdomyolysis is a pathology defined as a syndrome of acute renal failure, that is, it is configured as a set of signs and symptoms that arise when lysis of the skeletal striated muscle occurs, with the release of various substances from the intracellular content to the extracellular environment, with myoglobin being one of them and considered the main responsible for the toxic consequences of the disorder, resulting in electrolyte changes and elevation of serum creatinine, 4 to 5 times above the standard upper limit value. AGUIAR DT, et al., 2015; ALMEIDA JP, et al., 2020; NETO MP, et al., 2018; SANTANA NO and GOIS AFT. 2013; VERDOLIN LD, et al., 2013).

The pathophysiology of the disease described is not very well defined, but it involves infrarenal vasoconstriction and direct tubulotoxicity induced by the heme group of myoglobin and obstruction of the tubular flow by myoglobin, generating a symptomatic and laboratory picture of hypocalcemia, hypermagnesemia, hyperuricemia, hyperphosphatemia and hyperkalemia. (ROMANO TG, 2013)

The myocyte, a cell from muscle tissue, has the role of ensuring the maintenance of the ionic gradient that is made through transmembrane transport proteins (PTT), which depends on energy obtained from the degradation of ATP (adenosine triphosphate). In trauma or ATP decrease, damage occurs in the transport protein, proceeding in ionic imbalance, myocyte lysis, activation of protease, phospholipases and the inflammatory cascade, consequently establishing a process of fibrosis and necrosis in the renal tubules, impairing their entire function. hemodynamics in the human body. (NETO MP, et al., 2018)

Its cause is multifactorial, with several factors that can trigger rhabdomyolysis,

including trauma, extensive surgeries, car accidents, hydroelectrolytic disturbance, prolonged intense physical activity, intoxication by substances, medications and drugs. Another cause that has been described in rhabdomyolysis is disseminated intravascular coagulopathy. This event causes the dissemination of thromboplastin, evolving with the production of microthrombus in the glomeruli and, therefore, the decrease in glomerular filtration. (AGUIAR DT, et al., 2015; MAO H, et al., 2021; MONIZ MS, et al., 2016; DAHER EF, et al., 2005)

The major cause currently recorded as triggering the condition of rhabdomyolysis is trauma, represented by 85% of cases, and its most unwanted complications, such as myoglobinuria-related kidney injury, represents 7% to 10% of cases of AKI. Acute Kidney Disease), generating a negative impact on the future of patients who developed such a consequence; (ROMANO TG, 2013)

In terms of intense physical exercise, the Brazilian army uses as effective preventive measures for rhabdomyolysis, the separation of the military according to those who are overweight and/or previously sedentary, gradually increasing exercises, weights and training intensity; in addition to being evaluated and closely monitored by a health professional. Military personnel who perform strenuous activities must have work-rest cycles during physical activities, and must be adapted to the climatic conditions of the environment. All departmental supervisors must be instructed on the prevention of muscle injuries, with attention to early signs of rhabdomyolysis due to excessive exertion or an exaggerated increase in ambient temperature. (PEREIRA F, et al., 2018)

Current studies have shown that changes in body temperature, resulting from other causes, whether or not related to physical exercise, may be associated

with rhabdomyolysis, such as: neuroleptic syndrome, malignant hyperthermia, which can trigger the condition.(ESCOLA DE SAÚDE OF THE ARMY, 2019)

The clinical picture of rhabdomyolysis can be asymptomatic or present as intense myalgia, asthenia, myoglobinuria, choluria and general electrolyte disturbance. In the laboratory, it is common to present a sudden elevation of creatine kinase (CPK), hyperkalemia, hypocalcemia, hyperuricemia, liver inflammation, and consequently trigger cardiac arrhythmias and even cardiac arrest (FABI M, et al., 2021; NETO MP, et al, 2018; PEREIRA F, et al., 2018; SANTANA NO and GOIS AFT. 2013).

The symptoms presented are due to the lesion that the skeletal striated muscle suffers, with the release of content from the intracellular environment to the extracellular environment, as mentioned above. In addition to myoglobin, other enzymes such as aspartate aminotransferase (AST), aldolase, creatine phosphokinase (CPK), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH), phosphorus (P), potassium (K) and uric acid are released. (NETO MP, et al., 2018).

Rhabdomyolysis is considered a rare disease and must be considered a serious concern, which may result in hospitalization in order to prevent serious damage such as disseminated intravascular coagulation, cardiac arrhythmias, acute tubular necrosis and acute kidney injury. (ALMEIDA JP, et al., 2020).

Acute kidney injury resulting from rhabdomyolysis is a complication commonly found in patients hospitalized in an intensive care unit (ICU), and is characterized by a reduction in the glomerular filtration rate and/or urinary output, coursing with an overload of body fluids, a disorder hydroelectrolytic and acid-base levels and

decreased excretion of nitrogen compounds. In addition, the longer the hospitalization time, the greater the risk of deaths and complications. (BUTKUS JM, et al., 2021; MEYER M, et al., 2017).

To date, the ideal treatment for ARI caused by myoglobulins, what has been seen in many studies is volume expansion, but there is no rule on the amount of volume needed to be administered. Other measures such as urine alkalization to a pH lower than 6.5, forced diuresis with mannitol or loop diuretic require more rigorous monitoring in relation to the dosage of electrolytes such as calcium and potassium throughout the treatment. (ROMANO TG, 2013).

In some of the referenced texts, it was studied that the prognosis is variable, depending on the clinical condition that the patient presents, as well as the way his body reacts to the treatment carried out by the medical team. The individuals who had a poor prognosis were those whose myoglobinuric acute kidney injury were dialysis-dependent, resulting in increased mortality rates, being higher than those who did not depend on dialysis treatment. The indication for this procedure is acute kidney injury associated with metabolic acidosis and hyperkalemia, refractory to conservative treatment. (ROSA NG, et al., 2005).

In view of the above scenario, the question that guided the research was raised: What is the pathophysiology of rhabdomyolysis and why should it be considered a difficult-to-manage disease? This research aims to identify the relationship between prevention, treatment and diagnosis for the future, having boosted the study carried out between the period from 2016 to 2021.

## METHODS

Data on cases of rhabdomyolysis were collected through tracking information in the

Information System of Notifiable Diseases (SINAN) database, dating from January 2017 to December 2021, the survey was carried out in order to collect references recorded according to the aspect of hospitalizations by race/ethnicity, sex and type of care (emergency and elective) in the State of São Paulo. From the SINAN records, an investigation and data collection was carried out through tables and analysis of the results obtained.

Bibliographic analyzes were carried out by searching articles published in databases such as Medline, Scielo, Pubmed, Lilacs, Google Scholar and Cochrane library. The keywords used were: rhabdomyolysis, acute renal failure, emergency, high-impact physical exercise, crossfit, prolonged hospitalization and tubular necrosis. The investigation of the articles registered in the references was carried out from January 2022 to March 2022.

Studies were included, which after questioning and reading titles, abstracts and discussions could positively contribute to the development of the writing of this article. National texts were prioritized in the search for articles due to the similar treatment available and environmental factors, but

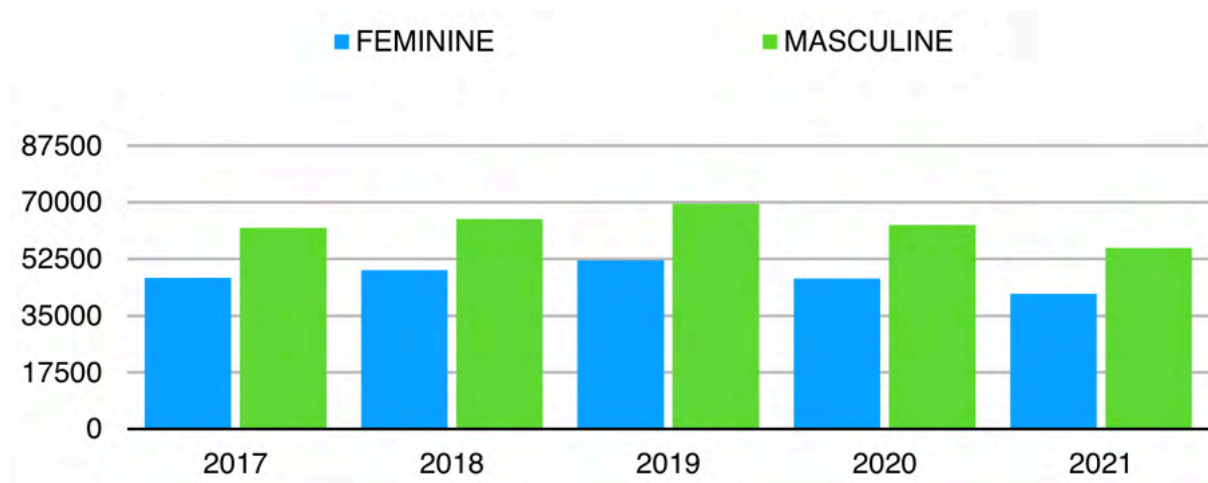
international texts were used that could add useful information for the development of new references. Works with very similar and repeated information were discarded, and the most current ones were selected. Paid texts or texts that were not presented in full were also excluded from the research.

This way, the study of this article has a descriptive approach, which aims to detail the behavior of a certain population or phenomenon, or even to stipulate a relationship between the variables, using the way of comparison, which makes it possible to identify similarities and differences between elements of a given region. (GIL AC, 2010)

Data processing and analysis were generated by frequency measurements observed with the DATASUS TabNet program. According to the SINAN records, a data collection was carried out in months and the analysis of the results obtained were made in years, considering the state of São Paulo in the period from 2017 to 2021.

## RESULTS/DISCUSSION

It is found in graphic 1 that hospitalizations according to gender, males had the highest



Graphic 1- Hospitalizations by gender from 2016 to 2021.

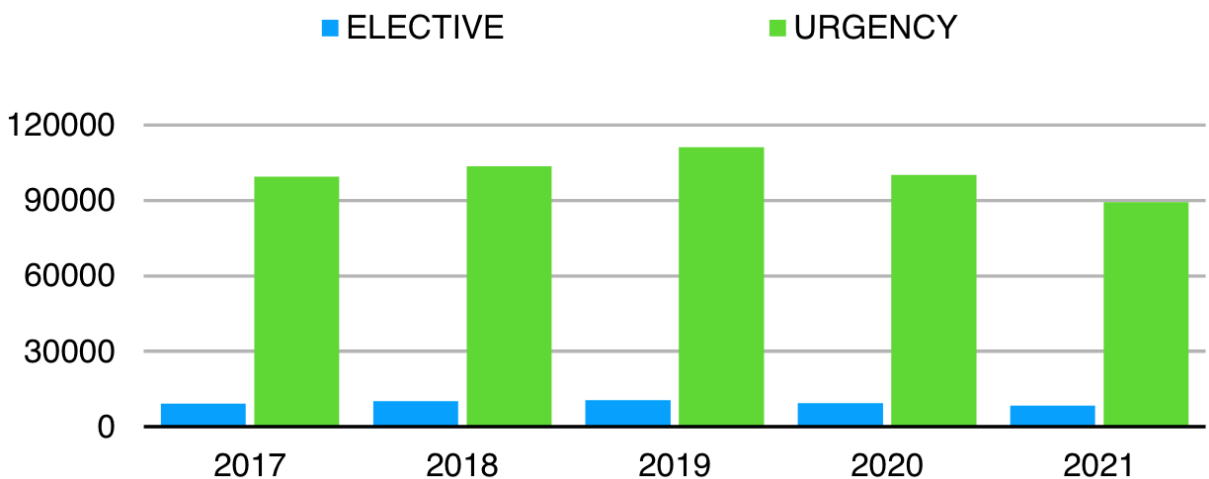
Source: GUIMARÃES CS, et al., 2021; data extracted from DATASUS, 2022.

incidence in all years, standing out in 2019 with 69,594 cases. Its lowest number was in the year 2021 with 55,976 numbers of attendances, decreasing by 13,618 numbers of cases. On the other hand, females have the lowest numbers of hospitalizations, the lowest indicator was in 2021 with 41,781 events. The highest number of hospitalizations was in 2019, with 52,077 cases. The number of hospitalizations due to rhabdomyolysis decreased by 10,296 numbers. It can be explained due to the fact that women are more cautious in traffic, thus avoiding an increasing number of car accidents, they are also more careful when it comes to health, exercising daily with consideration of the intensity of physical exercise and with help of trained health professionals. Women seek medical care early and periodically, thus having laboratory tests up to date, maintaining regular follow-up in health services, preventing and taking care of diseases early.

It is noted that male patients have high rates of hospitalizations for rhabdomyolysis, this is because they are associated with intense physical activity, and have the highest numbers

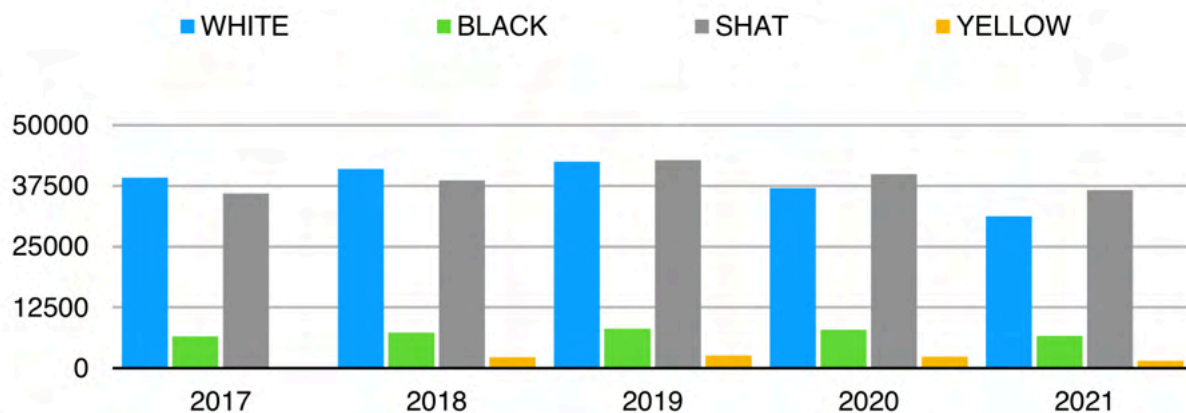
of car accidents, especially when related to motorcycles. Due to the high speed, and the lack of protection that drivers and passengers undergo in the vehicle, which during the collision there is the deceleration of the human body, causing the physical structure to receive the full impact of the shock, it has the whip movement of the head, that despite the skull protecting the brain, it can cause neurological damage. In addition, many muscle fibers end up being broken and releasing their toxicity to the body, which when passing through the kidneys, can lead to acute kidney failure and therefore rhabdomyolysis, as explained above, causing a huge electrolyte imbalance throughout the body.

Based on the data presented in **Graph 2**, hospitalizations according to the type of care in the period from January of 2016 to December of 2021. It is observed that the highest incidence occurred in an emergency with 111,189 in 2019 and its lowest index in the year 2021 with 89,408 frames with a drop of 21,781 cases between these two years. In the period of 2020, there was a drop in the number of demand for the emergency service, totaling 100,095 new cases.



Graph 2 - Hospitalizations according to character of interaction from 2016 to 2021.

Source: GUIMARÃES CS, et al., 2021; data extracted from DATASUS, 2022.



Graph 3- Hospitalizations by color/ethnicity from 2016 to 2021.

Source: GUIMARÃES CS, et al., 2021; data extracted from DATASUS, 2022.

When reported in an elective setting, there is a lower demand for medical services. In 2017, there were 9,262 occurrences. In 2018 and 2019, there was an increase in attendances in elective clinics of 999 and 1220 cases respectively, totaling 10261 and 10482 respectively. The year 2020 and 2021 saw a drop in demand, resulting in a total of 9,428 and 8,349 events in due order.

With this it is evident to relate that the medical search is associated with the initial signs and symptoms of the clinical picture of rhabdomyolysis that worries the patients, mainly with the darkening of the urine (choloria - presence of hemoglobin and protein) and the intense muscular pain, (this occurs due to the high rate of muscle fiber breakage and the release of myocytes into the bloodstream), thus, the signs and symptoms of the condition make them seek emergency medical care immediately and not a scheduled and scheduled appointment. It is clear that in every year of the research interval, the demand for urgency/emergency ends up being greater when compared to the demand in the elective sector.

In **Graph 3**, hospitalizations according to color/ethnicity dated from the first day of the

year 2016 to the last day of the year 2021 are seen. It is portrayed based on the recorded data, the color and ethnicity that most obtained the diagnosis of rhabdomyolysis was the brown with 193,973 of the cases, between the year 2017 and the year 2021. The reason for the result was sought in several studies and there was no effective clarification to justify such repercussion, noting that the white and brown population shared the top, which could be considered the a better social, educational and cultural condition, but without more precise and coherent explanations.

Thus, it is noted in the chart above that in 2017, the white race had the highest rate of patients diagnosed with rhabdomyolysis, this being 39,233, in the same year the brown race had a number of 35907 cases, the yellow race had 1,775 of the cases being the lowest number considered that year. In 2018, white continued to be the ethnicity with the highest number of cases that year, containing 40,975 patients, brown with 38,645 and yellow with 2,289, always being considered the lowest rate. In 2019, it obtained 42,849 of the cases diagnosed in browns, the white race was the second most affected, with a total of 42,485 cases and 2,611 in the yellow race, in the

change of decade and in the following year they kept the same races at the top and at the end of the year. classification being that in 2020, 39,899 in the brown population, 37066 in white and 2,374 in yellow in 2021 with 36,673 in brown and brown, 31256 in white and stalls and 1,480 in yellow, yellow.

It is evident that to reduce the morbidity and mortality of patients with Acute Renal Necrosis (ARN) it is necessary to have physiological control and adequate clinical support. The kidney is sensitive to hypoperfusion, with renal failure being the most common hemodynamic instability. Its renal medullary oxygenation is regulated by factors that control the supply and consumption of oxygen, and its failure directly affects the thick ascending limb or proximal segments, consequently decreasing renal blood flow by approximately 40-50% of the reference value, in addition to Furthermore, myoglobin dissolved in the extracellular medium after muscle lysis can induce the release of free iron through the heme fraction, which will catalyze the production of free radicals, further increasing the ischemic damage of the nephrotic tubules. In order for renal protection to occur after traumatic mechanisms, it is necessary to have three strategies, namely: venous hydration, maintenance of renal perfusion and urinary output (which is 0.5mL/Kg.min), so that it can avoid tubular obstruction and alkalinization. of urine with bicarbonate. (SANTOS LM et al., 2006; DAHER EF, et al. 2005).

According to Santos LM et al. (2006) in their work Renal Protection in the Surgical Intensive Care Unit (2006), it is recommended to measure urinary pH every 6 hours in those patients with CK > 5000 IU/L associated with the administration of bicarbonate in boluses, with the objective of maintaining urinary pH  $\geq$  8.0 in order to alkalinize the urine and decrease the chance of intratubular

myoglobin precipitation. In an intensive care unit (ICU) environment, medications that reduce glomerular perfusion pressure, such as converting enzyme inhibitors (ACEI) and all non-steroidal anti-inflammatory drugs (NSAIDs) must be avoided. The recommendation is then to achieve and maintain the patient's normovolaemia so that there is efficient renal protection and reduce factors that may contribute to renal dysfunction, post trauma.

## CONCLUSION

The objective of studying rhabdomyolysis is to understand and have a better defined pathophysiology, with this it is possible to affirm the importance of having more bibliographic studies and case reports that bring this definition to a better adaptation of diagnosis and favorable treatment for the sick, facilitating their management and diagnosis, thus avoiding this difficulty in the face of the exposed scenario. The study, however, was able to identify possible prevention of this pathology, such as: avoiding prolonged bed rest when the patient is hospitalized, reducing the practice of high-performance exercises when there is no effective hydration, or when just coming out of a sedentary lifestyle, avoiding temperatures very high or low, self-medication, drug or medication intoxication and caution in a traffic environment in order to avoid car accidents.