British Journal of Nursing

The management and diagnosis of rhabdomyolysis induced acute kidney injury: a case study.

--Manuscript Draft--

Manuscript Number:	bjon.2022.0142
Full Title:	The management and diagnosis of rhabdomyolysis induced acute kidney injury: a case study.
Article Type:	Case study
Keywords:	Rhabdomyolysis, acute kidney injury, treatment, management
Abstract:	Rhabdomyolysis is characterised by a rapid dissolution of damaged or injured skeletal muscle which can be caused by a multitude of different mechanisms. It can range in severity from mild to severe leading to multi organ failure and death. Rhabdomyolysis causes muscular cellular breakdown which can cause fatal electrolyte imbalances and metabolic acidosis, as myoglobin, creatine phosphokinase, lactate dehydrogenase and other electrolytes move into the circulation. This article will reflect a real case, who was diagnosed with rhabdomyolysis and acute kidney injury, after a fall at home. By understanding the underpinning mechanism of rhabdomyolysis and the associated severity of symptoms may improve early diagnosis and initiation of treatment.

The management and diagnosis of rhabdomyolysis induced acute kidney injury: a case study.

Abstract:

Rhabdomyolysis is characterised by a rapid dissolution of damaged or injured skeletal muscle which can be caused by a multitude of different mechanisms. It can range in severity from mild to severe leading to multi organ failure and death. Rhabdomyolysis causes muscular cellular breakdown which can cause fatal electrolyte imbalances and metabolic acidosis, as myoglobin, creatine phosphokinase, lactate dehydrogenase and other electrolytes move into the circulation. This article will reflect a real case, who was diagnosed with rhabdomyolysis and acute kidney injury, after a fall at home. By understanding the underpinning mechanism of rhabdomyolysis and the associated severity of symptoms may improve early diagnosis and initiation of treatment.

Introduction

This case study gives a detailed narrative of the aetiology; epidemiology and pathophysiology of rhabdomyolysis associated acute kidney injury (AKI), critically evaluating current evidence, to identify best practice through the use of a clinical case study (outlined in table 1). Clinical history taking, physical examination skills and laboratory investigations, will be explored as the most influential tools to exclude differential diagnoses (Balogh, Miller & Ball 2015), emphasising that accurate diagnosis and improved clinical outcomes must include a multispectral holistic assessment, in combination with diagnostic tools and treatment methods. Understanding the underpinning mechanism of rhabdomyolysis induced AKI and the associated severity of symptoms may improve early diagnosis and initiation of treatment.

What is rhabdomyolysis?

Rhabdomyolysis is a clinical syndrome which is characterised by a rapid dissolution of damaged or injured skeletal muscle (Kuijt et al 2021). According to Hirsch (2007) the disintegration of muscle can be caused by a multitude of different mechanisms that influence the integrity of the cells' plasma membrane, known as sarcolemma. The importance of the sarcolemma is that it provides a physical barrier between cells and external signals, which maintains the regulating process of cellular electrochemical gradients (Chatzizisis et al 2008). Therefore, the breakdown of the sarcolemma in rhabdomyolysis causes intracellular muscle components to move into the circulation (Lane and Phillips, 2003). The result of cell impairment is the release of myoglobin, creatine phosphokinase (CK), lactate dehydrogenase and other electrolytes (Kruijt et al 2021). McMahon et al (2013) emphasises that when progressive muscle damage manifests into development of rhabdomyolysis, the potential of fatal electrolyte imbalances and metabolic acidosis, increases significantly.

Rhabdomyolysis Syndrome

Ziam et al (2020) describe how rhabdomyolysis syndrome sits on a spectrum of severity, dependent on clinical presentation, underlying aetiology and associated risk factors rhabdomyolysis can be isolated to only asymptotic elevation of CK. In contrast, Hanif et al (2021) explain how severe cases of rhabdomyolysis can manifest into AKI, life-threatening conditions leading to multi-organ failure and death. Cabrel et al (2020) expands that the list of rhabdomyolysis myopathies is exhaustive, specifically separating into traumatic, non-traumatic and metabolic. Unfortunately, due to mild or absent symptoms, data and diagnosis for some myopathies are under reported

(Hohenegger, 2012) questioning the reliability and validity of research surrounding some areas of epidemiology.

Within the case study (Table 1), the patient had a prolonged immobilisation of more than 6 hours following a fall. A combination of clinical history, presenting symptoms and interpretation of CK and Creatinine, informed a diagnosis of AKI stage 3, induced by rhabdomyolysis. The case study was admitted to a high dependency unit determined by the presence of metabolic acidosis and AKI stage 3 suggesting that the case study's condition was critical.

Risk Factors

Torres et al (2015) identified risk factors which accelerate the development and severity of rhabdomyolysis such as prolonged immobilisation. According to Basile (2012) rhabdomyolysis secondary to prolonged immobilisation is the most common cause of related hospital admissions with the highest mortality rate. The main mechanism is severe muscle ischaemia from compression damage, leading to deprivation of oxygen to muscle tissues (Huerta-Alardí, Varon and Marik 2004). However, Wongrakpanich et al., (2018) suggest that prolonged immobilisation cannot serve as an independent prognostic marker for development in rhabdomyolysis but emphasise that the susceptibility of rhabdomyolysis development is exacerbated by other aetiologies such as multi-comorbidity.

Explored within an epidemiological study by Cheah et al., (2019) are the associated risks versus outcomes of rhabdomyolysis in the elderly. Patients with pre-existing diabetes and hypertension developed adverse outcomes compared to those without these comorbidities. NICE (2015) postulate that this is due to existing compromised circulatory volume, which when combined with rhabdomyolysis, amplifies muscle

necrosis and adverse outcomes. Interestingly, both hypertension and diabetes were present in the case study past medical history, suggesting that this patient was more susceptible to the development of rhabdomyolysis.

Risk factors

Genetic conditions that predispose rhabdomyolysis development include metabolic myopathies, muscular dystrophies, and channelopathies (Nance and Mammen 2015). Lahoria and Milone (2016) explain that many of these conditions are associated with exercise intolerance and rhabdomyolysis secondary to exertion. Therefore, although not present within the case study, amplifies the need for thorough and accurate history taking. Thus, it is important to determine whether there is baseline muscle weakness, a history of exercise intolerance particularly in association and development of disease processes.

Alongside inherited risk factors of genetics and co morbidity, pre-disposing medications are classed as an associated risk. Certain medications can cause metabolic disturbances specifically statins (Chatzizisis et al 2010). Statin induced myopathy can lead to the development of rhabdomyolysis due to the catabolism within the cell causing breakdown and secretion (Mamen 2016). Hilton-Jones (2018) highlights that this is particularly the case in older patients.

Importance of history taking

On history taking it was noted that the case study was prescribed Atorvastatin. However, the mechanism by which statins cause severe muscle necrosis and toxicity is not well understood, therefore the term statin-associated muscle symptoms (SAMS) is utilised to imply that these symptoms are not always truly caused by statin use

(Brunham et al., 2018). However, earlier research by Mendes et al (2014) emphasised that although approximately 10% of patients experience myalgia on a statin, the actual risk of rhabdomyolysis was low, specifically 1-2 cases for every 100,000 patients.

Methodical history taking for the clinical situation is essential in to reduce risk of rhabdomyolysis development, particularly vital when identifying and determining a diagnosis from other potential differentials. This notion is reinforced through historic and current studies (Saparadmadu et al 2021; Russel 2000; Cheah et al 2019). Good quality history taking is reliant on effective communication between the patient and practitioner, Cole and Bird (2014) emphasised that in order to refine the process of differential diagnosis, a focused and collaborative approach is paramount. In relation to this case study, obtaining an accurate history was difficult due to the patient's fluctuating level of consciousness due to their and acute illness thus impairing and challenging communication.

Acute Kidney Injury

The severity and mortality of rhabdomyolysis is exacerbated by the presence of AKI. De Meijer et al (2003) demonstrated that the associated mortality of patients admitted into Intensive Care Units (ICU) with rhabdomyolysis was 22% however, this increased to 59% if AKI was present. This is potentiated by the fact that 33% of all rhabdomyolysis cases develop an AKI with and a further 12% requiring ICU admission, including renal replacement therapy (McMahon, 2013). Conversely, Sawhney (2021) explains that no single factor can accurately predict AKI development in rhabdomyolysis.

Wczarek (2005) explains how Rhabdomyolosis induced AKI manifests from impaired glomerular filtration through three different ways, tubular obstruction, acute tubular injury and renal vasoconstriction. Petejova and Martinek (2014) associate renal tubular obstruction with excessive myoglobin. Extensive muscular damage causes substantive release of myoglobin into the blood stream (Holt and Moore 2000). Within normal pathophysiology myoglobin, the iron and oxygen binding protein support the conversion of oxygen to utilise into energy, this is then filtered via the kidneys and ultimately excreted via urine (Keltz et al 2013). However, in the presence of Rhabdomyolosis, myoglobin saturates the blood stream, causing cells to become overwhelmed (Block and Manning 2001). Myoglobin interacts with Tamm-Horsfall protein in the distal tubules and result in cast formation, obstructing renal tubules therefore decrease glomerular filtration (Blanco and Echeverria 2002). This is reiterated in Zager et al (2012) study which explains how the severity of tubular obstruction is exacerbated in hypovolaemia and acidosis due to increased concentration and acidic urine interaction. Both hypovolaemia and acidosis are aspects which were present within the case study, therefore suggesting tubular obstruction was exacerbated. However, the most significant indication of excessive myoglobin is 'brown coloured urine' known as myoglobinuria which was present within the case study.

Myoglobinuria

Cervellin et al (2010) define that myoglobinuria presents as a brown pigment which can be a visual sign of significant rhabdomyolosis, cell damage and likely associated tubular obstruction AKI. Hunter et al (2006) offers subjection to preliminary diagnoses from just 'brown coloured urine', expanding that urine changes depend on many factors such as the patient's muscle mass, severity of injury, urine concentration, and

renal function therefore is too subjective. Specifically, Keltz (2014) identifies how elevated plasma and urine myoglobin testing may be used in the early stages of the syndrome to support diagnosis. This is however conflicted within the case study as serum myoglobin levels were low. Basile, Anderson and Sutton (2012) explain how Myoglobin increases approximately 2 to 3 hours after muscle damage and peak levels at 8 to 12 hours post injury. However, because of its rapid excretion and metabolism to bilirubin, serum levels may return to normal much quicker (Mikkelsen and Toft 2005). Highlighting that it is not unusual for CK levels and 'brown urine' to remain elevated in the absence of serum myoglobin.

Mendes et al (2014) explain that excessive myoglobin also has a direct nephrotoxic effect, causing acute tubular injury (ATI). Necrosis of renal tubules affects the adequacy of filtration (Petejova and Martinek 2014). Hanif et al (2021) expands that renal vasoconstriction and hypovolaemia is a pathogenesis of severe AKI. Reduced renal blood flow activates the renin-angiotensin system (RASS) leading to renal vasoconstriction (Vanholder 2000). Therefore, a low circulating volume concludes to decreased kidney function. In addition, Kellum et al (2021) highlights the association with acute tubular injury (ATI), acknowledging that prolonged hypoperfusion of the kidney accelerates to necrosis of nephron tubules. Basile, Anderson and Sutton (2012) agree that renal vasoconstriction is a leading cause for majority of AKI. Hypotension and hypovolaemia are both conclusions from the fluid assessment undertaken within the case study. However, additional finding within examination was bilateral peripheral oedema. NICE (2017) argues that bilateral pitting oedema is a clinical sign of fluid overload. This highlights the significance of accurate fluid balance assessment and documentation, requiring the collaborative approach between the

medical team and ward nurses as any error in correction hypovolaemia has significant adverse effects to AKI recovery.

Peripheral oedema

Ejikeme et al (2021) report that peripheral oedema bilaterally collating within arms and leg is cited within many case reports of Rhabdo. Anderson and Sutton (2012) suggests that this is due to the imbalance of extravascular fluid and intravascular depletion explaining that a rhabdomyolosis diagnosis adds an additional complexity of sequestration or 'third' spacing' of fluids into injured muscles. Torres, Helmstetter and Kaye (2015) expand that the release of cellular constituents from damaged muscles lead to a number of imbalances particularly metabolic acidosis, hyperkalaemia, hypophosphataemia and hyperuricaemia therefore triggers secondary activation of the RASS system, stimulating accumulation of fluid within the extravascular space (Roumelioti et al 2018).

In application to the case study, it could be argued the pathophysiology of AKI through rhabdomyolosis had an element of all three; renal vasoconstriction, tubular obstruction and ATI. Waikar et al (2018) state that accurate exploration of mechanisms of intrinsic AKI, require a kidney biopsy. However, within an acute setting is argued to be high risk of bleeding, inappropriate and too subjective to add clinical value to management (Waikar and McMahon 2018).

Symptoms

Cervellin et al (2010) describes a classic triad of rhabdomyolosis symptoms specifically oliguria of 'Brown' coloured urine, acute/subacute myalgia and weakness. All three of these symptoms were expressed within the clinical presentation of the case

study. Remarkably however, Torres, Helmstetter and Kaye (2015) argues that these are present concurrently in less than 10% of cases. Additional generalised systemic symptoms reported alongside similar presentation of Rhabdo include fever, general malaise, tachycardia, nausea and vomiting (Huerta-Alardín et al 2004). Bagley et al (2007) suggests that diagnosis rests upon the presence of a high level of suspicion of any abnormal laboratory values in the mind of the treating physician.

The hallmark of rhabdomyolosis is an elevation in CK. Serum CK level is argued the most sensitive laboratory finding pertaining to muscle injury and is used within current practice (Leverenz et al 2016). Clinical diagnoses is based on threshold of 10 times the upper limit of normal (1,000 IU/L). Within the case study explored, the initial CK was 1200, and progressed to peak at 24000, 48hr from admission. According to Al-Hadi and Fox (2009) serum CK begins to rise within 2 to 12 hours following the onset of muscle injury and reaches its maximum within 24 to 72 hours. Subsequently a decline is usually seen within three to five days of cessation of muscle injury, if adequate treatment is given (Keltz, Khan and Mann 2014). Moghadam-Kia et al (2016) add caution to this algorithm, explaining that in patients with chronic muscle diseases or genetic conditions may already have chronically elevated CK levels. Therefore, in this cohort of patients, CK trends and comparison should inform diagnosis, emphasising a holistic evaluation when informing diagnosis (Zimmerman 2013).

Differential diagnoses

Other differential diagnoses should be considered in which the presence of myalgia, elevated CK and dark urine exist. For example, patients with inflammatory myopathy may also exhibit myalgia, elevated CK and exhibit Myoglubinuria (Cervellin, Comelli and Lippi 2010). However, these patients can be differentiated from patients with

rhabdomyolosis by the assessing practitioner, via a thorough history exploring the chronicity of symptoms. Dimachkie and Barohn (2012) clarify that usually symmetric proximal muscle weakness due to inflammatory myopathy develop over weeks to months whereas patients with rhabdomyolosis present with an acute deterioration associated to an event. Extensive evidence exists whereby serum CK rises acutely with myocardial infarction (MI) (Mannix et al 2006). However, in contrast to MI patients, rhabdomyolosis is not directly associated with ischaemic chest pain nor abnormal changes to electrocardiogram (ECG).

Diagnosis

When the triad of symptoms, laboratory and history present together, and if the CK elevation is acute and myoglubinuria is present, the diagnosis of rhabdomyolosis can be made with confidence. The aforementioned differentials may be considered, depending upon the combination of findings that are present, but distinctions can usually be made with readily available information from the medical history as well as the physical and laboratory results.

Treatment

Torres et al (2015) explains that rhabdomyolosis induced AKI primary treatment goals are to preserve renal function and restoring metabolic derangements. The underlying aetiologies such as hypovolaemia, hypotension and tubular obstruction should be treated with early and adequate volume replacement (Hanif et al 2014). Volume expansion increases renal blood flow and consequently glomerular filtration, conflicting research exists on specific type and volume of intravenous fluid should be used (Keltz et al 2014). Within the case study described initial treatment was 0.9% normal saline to support fluid resuscitation. One study by Cho et al (2007) compared

normal saline and lactated Ringer's for serum potassium or CK clearance. Interestingly, findings sought no significant weighting difference. Additionally, research by Lobo and Awad (2014) suggest there is an optimum level of normal saline which should be monitored, placing specific focus to chloride concentrations and increasing risk of hyperchloraemic metabolic acidosis.

Additionally, NICE (2018) emphasise that careful monitoring is essential due to cardiopulmonary risk factors specifically large fluid infusion can lead to congestive heart failure and pulmonary oedema. Therefore, conflicting evidence exists. Due to the multifactorial considerations required in managing metabolic derangements and extravascular versus intravascular fluid demand. Consideration should be made to electrolytes results, clinical volume status examinations and laboratory results in order to inform optimum fluid constitutes, rather than having a blanket approach to all cases.

Rhabdomyolosis is associated with decreased urinary pH specifically acidosis. Efstratiadis et al (2007) defines how this can further result in myoglobin precipitation and obstruction. Wider reading has identified sodium bicarbonate being used in addition to fluid replacement in rhabdomyolosis management (Somagutta et al 2020) as it aids alkalinisation of the urine and assists to prevent cast formation through crystallisation of uric acid, thereby reducing AKI risk (Michelsen et al 2019). However, Valette et al (2017) explain that there are no randomised controlled trials which evidence the benefit in improving AKI, preventing acute dialysis, or influence mortality when compared to aggressive fluid rehydration. Therefore, remains difficult to define sodium bicarbonate as an optimum Rhabdo treatment.

Loop diuretics, specifically furosemide, have also been reportedly used in Vanholder (2000) study for forced diuresis. However, this has not demonstrated benefit when

compared to fluid resuscitation alone. Specifically, Efstratiadiset al (2007) argues that loop diuretics can worsen urine acidosis. Evidence does not demonstrate improved mortality, need for dialysis, or hospital length of stay when furosemide was used in patients with AKI and Rhabdo. Therefore, the use of diuretics in such patients is debatable, as limited evidence exists in favour of their role in improving outcomes.

Multidisciplinary team communication

Verbal and written communication with the multidisciplinary team is crucial in management to optimise treatment (Frassetto, 2018). In this case, discussions between the nursing staff and medical team were necessary to ensure fluid and medication prescriptions were being adhered to. The teamworking of nursing staff is vital in order to monitor improved patient condition. Appropriate escalation is paramount to effective fluid status optimisation, constant feedback and communication to monitor response to treatment, oliguria and any deterioration (NICE 2015).

Within the case study, collaborative relationships were formed to support family members due to the patient's labile condition and risk for deterioration. Aligning with patient and family wishes, values and beliefs was crucial to inform early decisions (De Decker et al., 2012). A discussion took place in regard to ceiling of treatment, resuscitation decision and realistic explanation of prognosis and recovery. Ahearn et al., (2010) explain that this type of communication allows the predetermined highest level of intervention deemed appropriate to be outlined by a medical team. Walzl et al., (2019) research suggests that the presence of a strong working relationship with the nursing team helps improve patient and family experience of life changing medical conditions and the dying process. De Decker et al (2012) add that such discussions

improve the recognition and allowance of natural death, whilst avoiding futile life sustaining treatments.

Careful fluid resuscitation and fluid status optimisation is vital to enhance a recovery process. Complications of prolonged rhabdomyolosis and un-resolving AKI exist, particularly acute haemodialysis. Temporary 'rescue' dialysis treatment may be offered in the most severe of cases to aid removal of nephrotoxic substances and correction of the electrolyte abnormalities (Torres et al., 2015). Evidence exists the early initiation of dialysis in patients with rhabdomyolosis may improve the outcome of kidney injury (Candela et al., 2020; Petejova et al., 2014).

It would be helpful to know what happened to the patient

Conclusion

Current research regarding the aetiology and presentation of rhabdomyolosis induced AKI is expansive, however no current guidelines for 'gold standard' management exist. The presentation of rhabdomyolosis induced AKI can present a myriad of different ways to an assessing practitioner, although, themes of presenting symptoms exist. This emphasises the importance of quality history taking combined with refined physical examination skills and interpretation of laboratory investigation. Balogh, Miller & Ball (2015) identifies these as the two most influential means to exclude differential diagnoses, concluding that the management of rhabdomyolosis requires a collaborative and multidisciplinary approach to management to reduce associated risk of adverse outcomes.

Reference List

Ahearn, D., Jackson, T., Melimovie, J., Weatherburn, A. (2010) 'Improving end of life care for nursing home residents: an analysis of hospital mortality and readmission rates', **Postgraduate Medical Journal,** 86(1013), pp.131–135

Al-Hadi, H., Fox, K. (2009). 'Cardiac markers in the early diagnosis and management of patients with acute coronary syndrome', **Sultan Qaboos University medical journal**, 9(3), pp. 231–246.

Bagley, W., Yang, H., Shah, K. (2007) 'Rhabdomyolysis', **Internal and Emergency Medicine,** 2, pp. 210-218

Balogh, E., Miller, B., Ball, J. (2015) **Improving Diagnosis in Health Care**. Washington: The National Academies of Sciences, Engineering, and Medicine.

Basile, D., Anderson, M., Sutton, T. (2012). 'Pathophysiology of acute kidney injury', **Comprehensive Physiology**, 2(2), pp. 1303–1353.

Brunham, L., Baker, S., Mammen, A., Mancini, G., Rosenson, R. (2018) 'Role of genetics in the prediction of statin-associated muscle symptoms and optimization of statin use and adherence' **Cardiovascular Research**, 114(8), pp. 1073.

Bruso, J., Hoffman, M., Rogers, I., Lee, L., Towle, G., Hew-Butler, T. (2010) 'Rhabdomyolysis and hyponatremia: a cluster of five cases at the 161-km 2009 Western States Endurance Run', **Wilderness & Environmental Medicine,** 21(4), pp. 303-308.

Cabral, B., Edding, S., Portocarrero, J., Lerma, E. (2020) 'Rhabdomyolysis', **Disease-a-Month,** 66(1).

Candela, N., Silva, S., Georges, B. Claire Cartery, C., Robert, T., Moussi-Frances J., Rondeau, E., Rebibou, J., Lavayssiere, L., Belliere, J., Krummel, T., Lebas, C., Cointault, O., Sallee, M., Fague, S. (2020) 'Short- and long-term renal outcomes following severe rhabdomyolysis: a French multicenter retrospective study of 387 patients', **Annals of Intensive Care,** 10(27), DOI: https://doi.org/10.1186/s13613-020-0645-1

Cervellin, G., Comelli, I. and Lippi, G. (2010) 'Rhabdomyolysis: historical background, clinical, diagnostic and therapeutic features', **Clinical Chemistry and Laboratory Medicine**, 48(6), pp. 749-756.

Cervellin, G., Comelli, I., Lippi, G. (2010) 'Rhabdomyolysis: historical background, clinical, diagnostic and therapeutic features', **Clinical Chemistry and Laboratory Medicine,** 48(6), pp.749-756.

Charman, E., Troutman, W. (2013) 'Prevention of kidney injury following rhabdomyolysis: a systematic review', **Annals of Pharmacotherapy,** 47(1), pp. 90-105.

Chatzizisis, Y., Koskinas, K., Misirli, G., Vaklavas, C., Hatzitolios, A., Giannoglou, G.(2010**) '**Risk factors and drug interactions predisposing to statin-induced myopathy: implications for risk assessment, prevention and treatment', **Drug Safe,** 33(3), pp. 171-187.

Chatzizisis, Y., Misirli, G., Hatzitolios, A., Giannoglou, G. (2008) 'The syndrome of rhabdomyolysis: Complications and treatment', **European Journal of Internal Medicine,** 19, pp.568–570. DOI:10.1016/j.ejim.2007.06.037.

Cheah, S., Isahak, M., Wan Mat, W., Ping Tang, S., Teo, R., Yusof, A ., Rahman, R. (2019**) '**Case report: a fatal case of severe pancreatitis associated with rhabdomyolysis', **Critical Care and Shock,** 2(5), pp. 275-280.

Cho, Y., Lim, H., Kim, S. (2007) 'Comparison of lactated Ringer's solution and 0.9% saline in the treatment of rhabdomyolysis induced by doxylamine intoxication', **Emergency Medical Journal,** 24(4), pp. 276-280.

De Decker, L., Beauchet, O., Gouraud-Tanguy, A., Berrut, G., Annweiler, C., Le Conte, P. (2012) 'Treatment-limiting decisions, comorbidities, and mortality in the emergency departments: A cross-sectional elderly population-based study', **Journal of Nutrition Health and Aging,** 16, pp. 914–918.

De Meijer, A., Fikkers, B., De Keijzer, H., Van Engelen, B., Drenth, J. (2003) 'Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey', **Intensive Care Medicine,** 29, pp. 1121–1125. DOI: https://doi.org/10.1007/s00134-003-1800-5.

Dimachkie, M., Barohn, R. (2012) 'Idiopathic inflammatory myopathies', **Semin Neurology,** 32(3), pp.227-236. DOI:10.1055/s-0032-1329201.

Efstratiadis, G., Voulgaridou, A., Nikiforou, D., Kyventidis, A., Kourkouni, E., Vergoulas, G.(2007) 'Rhabdomyolysis updated'. **Hippokratia**, 11(3), pp.129-137.

Efstratiadis, G., Voulgaridou, A., Nikiforou, D., Kyventidis, A., Kourkouni, E., Vergoulas, G. (2007) 'Rhabdomyolysis updated', **Hippokratia,** 11(3), pp.129-137.

Ejikeme, C., Alyacoub, R., Elkattawy, S., Shankar, T., Yuridullah, R. (2021) 'A Rare Complication of Rhabdomyolysis: Peripheral Neuropathy', **Cureus,** 13(3).

Gabow, P., Kaehny, W., Kelleher, S. (1982) 'The spectrum of Rhabdomyolosis', **Medicine (Baltimore),** 61(3), pp. 141-52.

Hanif,M., Bali, A., Ramphul, K. (2021) *Acute Renal Tubular Necrosis.* **T**reasure Island:Stat Pearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK507815

Hilton-Jones D.(2018) 'Statin-related myopathies' **Practice Neurology,** 18, pp. 97–105.

Hirsch, N (2007) 'Neuromuscular junction in health and disease', **British Journal of Anaesthesia**, 99, pp. 132–138. DOI: 10.1093/bja/aem144.

Hohenegger, M. (2012) 'Drug induced rhabdomyolysis', **Current opinion in pharmacology,** 12(3), pp. 335–339. https://doi.org/10.1016/j.coph.2012.04.002

Holt, S., Moore, K. (2000) 'Pathogenesis of renal failure in rhabdomyolysis: the role of myoglobin**', Clinical and Experimental Nephrology**, 8(2), pp.72-76.

Huerta-AlardínA., Varon J., Marik P. (2004) 'Bench-to-bedside review: Rhabdomyolysis – an overview for clinicians', **Critical Care,** (9)158.

Hunter, J., Gregg, K., Damani, Z. (2006) **'**Rhabdomyolysis', **Continuing Education in Anaesthesia, Critical Care & Pain,** 6(4).

Kellum, J., Romagnani, P., Ashuntantang, G., Ronco, C., Zarbock, A., Anders, H. (2021) 'Acute kidney injury', **Nature Review Disease Primers,** 7(52).

Keltz, E., Khan, F., Mann, G. (2014). 'Rhabdomyolysis. The role of diagnostic and prognostic factors', **Muscles, ligaments and tendons journal**, 3(4), pp. 303–312.

Keltz, E., Khan. F., Mann, G. (2014) 'Rhabdomyolysis. The role of diagnostic and prognostic factors', **Muscles, ligaments and tendons journal,** 3(4), pp. 303–312.

Kruijt, N., Van den Bersselarr, L., Kamsteeg, E., Verbeeck, W., Snoeck, M., Everaerd, D., Abdo, W., Jansen, D., Erasmus, C., Jungbluth, H., Voermans, N. (2021) 'The etiology of rhabdomyolysis: an interaction between genetic susceptilitity and external triggers', **European Journal of Neurology,** 28, pp. 647-659. DOI:10.1111/ene.14553.

Lahoria, R., Milone, M. (2016) 'Rhabdomyolysis featuring muscular dystrophies', **Journal of Neurological Science**, 15(361), pp. 29-33. DOI: 10.1016/j.jns.2015.12.013.

Lane, R., Phillips, M. (2003) 'Rhabdomyolysis Has many causes, including statins, and may be fatal', **The British Medical Journal,** 327(7407), pp. 115–116. DOI: 10.1136/bmj.327.7407.115.

Leverenz, D., Zaha, O., Crofford, L., Chung, C. (2016) 'Causes of creatine kinase levels greater than 1000 IU/L in patients referred to rheumatology' **Clinical Rheumatology,** 35(6), pp. 1541-1547.

Lobo, D., Sherif Awad, S. (2014) 'Should chloride-rich crystalloids remain the mainstay of fluid resuscitation to prevent 'pre-renal' acute kidney injury?', **International Society of Nephrology,** 86, pp. 1096–1105.

Mammen, A.(2016) 'Statin-Associated Autoimmune Myopathy' **New England Journal of Medicine**, 374(7), pp. 664-669.

Mannix, R., Tan, M., Wright, R., Baskin, M. (2006) 'Acute pediatric rhabdomyolysis: causes and rates of renal failure**' Pediatrics,** 118(5), pp. 2119-2125.

McMahon, G., Zeng, X., Waikar, S. (2013). 'A risk prediction score for kidney failure or mortality in rhabdomyolysis', **JAMA internal medicine**, 173(19), pp. 1821–1828.

Mendes, P., Robles, P., Mathur, S. (2014) 'Statin-induced rhabdomyolysis: a comprehensive review of case reports' **Physiotherapy Canada**, 66(2), pp. 124-132.

Mendes, P., Robles, P., Mathur, S. (2014) 'Statin-induced rhabdomyolysis: a comprehensive review of case reports' **Physiotherapy Canada**, 66(2), pp. 124-132. DOI: 10.3138/ptc.2012-65.

Michelsen, J., Cordtz, J., Liboriussen, L., Behzadi, M., Ibsen, M., Damholt,M . (2019) 'Prevention of rhabdomyolysis-induced acute kidney injury – A DASAIM/DSIT clinical practice guideline', **Scandinavian Society of Anaesthesiology and Intensive Care Medicine.** 63(5), pp.563-702.

Moghadam-Kia, S., Oddis, C., Aggarwal, R. (2016) 'Approach to asymptomatic creatine kinase elevation', **Cleveland clinic Journal of Medicine,** 83(1), pp. 37-42.

Nance, J., Mammen, A. (2015) 'Diagnostic evaluation of rhabdomyolysis', **Muscle Nerve**, 51(6), pp.793-810. DOI:10.1002/mus.24606

National Institute of Health and Care Excellence (NICE) (2015) *Older people with social care needs and multiple long-term conditions.* Available at: https://www.nice.org.uk/guidance/ng22 (Accessed : 1/1/22)

National Institute of Health and Care Excellence (NICE) (2016) *reports on Multimorbidity: clinical assessment and management.* Available at: https://www.nice.org.uk/guidance/ng56 (Accessed: 1/1/22)

National Institute of Health and Care Excellence (NICE) (2017) *Intravenous fluid therapy in adults in hospital*. Available at: https://www.nice.org.uk/guidance/cg174/chapter/1-recommendations (Accessed 08/03/22).

Petejova, N., Martinek, A. (2014) 'Acute kidney injury due to rhabdomyolysis and renal replacement therapy: a critical review', **Critical Care, 1(3) 224.**

Rawson, E., Clarkson, P., Tarnopolsky, M. (2017) 'Perspectives on Exertional Rhabdomyolysis', **Sports Medicine,** 47, pp. 33–49. DOI: 10.1007/s40279-017-0689-z.

Roumelioti, M., Glew, R., Khitan, Z., Rondon-Berrios, H, Argyropoulos, C., Malhotra, D., Agaba, E., Rohrscheib, M., Murata, G., Shapiro, J., Tzamaloukas, A. (2018) 'Fluid balance concepts in medicine: Principles and practice', **World Journal of Nephrology,** 7(1), pp. 1-28. DOI:10.5527/wjn.v7.i1.1.

Russell, T. (2000) 'Acute renal failure related to rhabdomyolysis: pathophysiology, diagnosis, and collaborative management**', Nephrology Nurses Journal**, 27(6), pp. 567-75.

Saparamadu, A., Teo, W., Arsad, A. (2021) 'Avoidable healthcare costs of spinning-induced rhabdomyolysis:a case series', **Internal Medicine Journal,** 51, pp. 1946-1949.

Sauret, J., Marinides, G., Wang, G. (2002) ‘Rhabdomyolysis’, **American Family Physician**, 65(5), pp. 907–912.

Sawhney, J., Kasotakis, G., Goldenberg, A., Abramson, S., Dodgion, C., Patel, N., Khan, M., Como, J. (2021) ‘Management of rhabdomyolosysis: A practice management guideline from the Easternn Association for the Surgery of Trauma’, **The American Journal of Surgery, DOI:https://doi.org/10.1016/j.amjsurg.2021.11.022.**

Somagutta, M., Pagad, S., Sridharan, S., Nanthakumaran, S., Arnold, A., May, V., Malik, B. (2020) ‘Role of Bicarbonates and Mannitol in Rhabdomyolysis: A Comprehensive Review.’ **Cureus,** 12(8), DOI:10.7759/cureus.9742. PMID: 32944457; PMCID: PMC7490772.

Stanley, M., Chippa, V., Aeddula, N., Rodriguez, B., Adigun, R. (2021) *Rhabdomyolysis.* Treasure Island: Stat Pearls Publishing.

Torres, P., Helmstetter, J., Kaye, A. (2015) ‘Rhabdomyolysis. Pathogenesis, Diagnosis, and Treatment’, **The Oschner Journal**, 15, pp. 58-69.

Torres, P., Helmstetter, J., Kaye, A. (2015) ‘Rhabdomyolysis: Pathogenesis, Diagnosis, and Treatment’, **Ochsner Journal,** 15(1), pp. 58–69.

Torres-Villalobos, G., Kimura, E., Mosqueda, J., García-García, E., Domínguez-Cherit, G., Herrera, M. (2003) ‘Pressure-induced rhabdomyolysis after bariatric surgery’, **Obesity Surgery,** 13(2), pp. 297–301.

Valette, X., Desmeulles, I., Savary, B., Masson, R., Seguin, A., Sauneuf, B., Brunet, J., Verrier, P., Pottier, V., Orabona, M., Samba, D., Viquesnel, G., Lermuzeaux, M., Hazera, P., Dutheil, J., Hanouz, J., Parienti, J., Cheyron, D.

(2017) ‘Sodium Bicarbonate Versus Sodium Chloride for Preventing Contrast-Associated Acute Kidney Injury in Critically Ill Patients: A Randomized Controlled Trial’, **Critical Care Medicine**, 45(4), pp. 637-644. DOI: 10.1097/CCM.0000000000002267. PMID: 28181941.

Vanholder, R., Sukru Sever, M., Erek, E., Lameire, N. (2000) ‘Rhabdomyolysis’, **Journal of the American society of Nephrology,** 11(8), pp. 1553–1561.

Waikar, S., McMahon, G. (2018) ‘Expanding the Role for Kidney Biopsies in Acute Kidney Injury’, **Semin Nephrology**, 38(1), pp. 12-20. DOI: 10.1016/j.semnephrol.2017.09.001.

Waikar, S., McMahon, G. (2018) ‘Expanding the Role for Kidney Biopsies in Acute Kidney Injury’, **Seminars Nephrology**, 38(1), pp. 12-20.

Walzl, N., Jameson, J., Kinsella, J. Lowe, D. (2019) ‘Ceilings of treatment: a qualitative study in the emergency department’, **BMC Emergency Medicine,** 19(9).

Wczarek, J., Jasińska, M., Orszulak-Michalak, D. (2005) ‘Drug-induced myopathies’, **Pharmacology Research,** 57, pp. 23–34.

Wongrakpanich, S., Kallis, C., Prasad, P., Rangaswami, J., Rosenzweig, A. (2018) ‘The Study of Rhabdomyolysis in the Elderly: An Epidemiological Study and Single Center Experience’, **Aging Disease Journal,** 9(1), pp. 1-7. DOI: 10.14336/AD.2017.0304.

Zager, R., Johnson, A., Becker, K. (2012) ‘Plasma and urinary heme oxygenase-1 in AKI’, **American Society of Nephrology,** 23, pp. 1048–1057. DOI: 10.1681/ASN.2011121147.

Zaim, S., Chong, J., Sankaranarayanan, V., Harky, A, (2020) 'COVID-19 and Multiorgan Response', **Current problems in cardiology,** 45(8). DOI:10.1016/j.cpcardiol.2020.100618.

Zimmerman, J., Shen, M. (2013) 'Rhabdomyolysis', **CHEST,** 144, pp.1058–1065.

Table 1- Case Study

Age: 78
Gender: Male
History of presenting complaint and symptom Admitted to High dependency unit from accident and emergency department after admission to hospital due to being found by a relative on the floor. Fallen in the night whilst trying to get out of bed to, lost balance but did not lose consciousness and has no obvious head injuries. Approximately spent minimum of 6 hours on the floor. **Presenting Symptoms** Mild confusion Hypotension Malygias Mulscle weakness and decreased mobility Oliguria - Concentrated 'brown urine' Requiring oxygen to meet saturations between 94-98% **Observations** BP: 85/45 HR: 105 RR:15 SATS: 95% Oxygen: 35% VFM Temp:39.0 **Examinations** **Fluid status** • JVP not raised • Tongue coated and dry mucus membrane

- Mild odema to lower limbs and forearms
- Oliguria < 100ml in 24hr concentrated and brown

Chest

- Reduced air entry and coarse crackles to left lower lung bases

Heart

- Normal heart sounds
- Regular Tachycardia

Past medical history

- Type two Diabetes Mellitus
- Chronic Kidney Disease Stage 2
- Hypertension
- Heart Failure

Drug history

Metformin	500mg	Twice Daily
Ramipril	2.5mg	Twice Daily
Folic Acid	5mg	Once Daily
Atorvastatin	20mg	Once Daily
Bisoprolol	5mg	Once Daily

Additional Medication- ‘ over the counter’

Paracetamol	1g	As and when required

Allergies –

No Known Drug Allergies

Social History

- Lives alone
- Family live Nearby
- No social support
- Normally independent with all activities of daily Living

Family History

- Chronic Kidney Disease
- Diabetes

Risks

- No Illicit Drug Use
- Non- smoker – quit smoking 30+ years prior
- Minimal alcohol intake ‘on special occasions’
- No Recent Travel

Differential Diagnosis(s)

- Inflammatory response to infection
- Cardiac ischemia, myocardial infarction

Potential management /referrals/communication

Laboratory investigations including inflammatory screen

- Flood Blood Count
- Urea and Electrolyte
- Liver Function Test
- C-reactive protein
- Blood Cultures
- Creatine Kinase

Imaging investigations

- Chest X-ray

- Regular fluid status assessment
- Rehydration Intravenous fluids
- Intravenous Antibiotics
- **communication to family to gain collateral history and to discuss treatment options, escalation management and ceiling of care**