**Background**

ICU patients are at risk of developing Hypophosphatemia (HP) and Refeeding Syndrome (RS) providing over nutrition to patient suspected with RS might be ended with fatal results. Preventing and early identification could be saving life. Inadequate conception about the nurse's role and responsibility in nutrition therapy may cause defective results.

**Objectives**

This study aimed to examine the knowledge and behaviors of intensive care unit (ICU) nurses in the case of hypophosphatemia and re-feeding syndrome and nutrition in general. We analyzed the correlation between the nurses' knowledge of these subjects to the rate HP in their unit, length of ICU stay, duration of mechanical ventilation, and mortality.

**Methods**

Data collection and analysis for this study were obtained during 2018 from 45 ICU (intensive care unit) nurses about their Hypophosphatemia (HP) and Refeeding Syndrome (RS) knowledge and their role in nutrition among ICU patients. Besides, data collected retrospectively included an observational study on 275 medical-surgical ICU patients. Data was withdrawn from the same unit were the participant nurses were working at.

**Results**

Analyses led to the importance of monitoring the patient's levels of phosphate and treating them accordingly. HP and RS can result in more complications such as length of hospitalization and length of mechanical ventilation. Besides, there is a correlation between the level of nurses' knowledge and there approach toward current nutrition guidelines, the higher the nurses' knowledge, the more he/she will follow the current nutrition guidelines.

**Conclusions**

The present study shows there is a direct influence of the nurses' knowledge to the patients' complications that resulted from HP and/or RF. Educate the ICU nurses in clinical nutrition is essential and part of critical care patient's treatment. This can be crucial to patients' outcomes and ultimately save the patient's life.

**Introduction:**

ICU patients oftentimes create electrolyte imbalance in general and hypophosphatemia in particular. Hypophosphatemia (HP) is a disruption in the body's phosphorus level, which is characterized by low levels of phosphorus in the bloodstream.(1) ICU patients have serious circumstances that put them at risk of developing hypophosphatemia, such as sepsis, acute respiratory alkalosis, diabetic ketoacidosis, levels of albumin and prealbumin as well as malnutrition and defective body phosphorus reservoir (1,2).

Hypophosphatemia is found to be highly correlated to Refeeding Syndrome (RS) (3). The main reason for Refeeding Syndrome is a process that occurs when undernourished individual eat carbohydrates, and as a result, insulin is released, which encourages glucose and phosphorus into the cells. RS is the abrupt imbalance of electrolytes through the intra-extracellular composition (4). Critically ill patients are at risk of adverse events during starting food deliveries (5).

Providing over nutrition to patient suspected with RS might be ended with fatal results. Preventing and early identification could be saving life (6).

Prevalence of RS varies across studies due to deficient in global definition and objective diagnostic criteria. RS ranging from 25% to 45% for ICU patients (4,6,7). The rate of RS might be even higher due to the fact that RS is underdiagnosed and therefore in many cases it is not reported (8). HP and RS is associated to longer hospitalization, impair outcomes and mortality (9) .

In case of HP, if the low phosphate levels are ignored by the nursing stuff and the patient is fed despite the low phosphate levels, this can lead to additional dangerous decrease in phosphates level, rapid changes in other electrolytes (RS) that can also result in death (5,10,11). Therefore, to provide effective nutritional treatment it is necessary to monitor the patients in the ICU (5).

According to Tagney & Haines (12), knowledge provide the nurse with the tools to function in varying patient care situations and to predict the outcomes of the desired intervention. In addition, as the nurse's knowledge is broader, the more inventive resources the nurse can rely on when needed, thereby providing knowledge-based care.

ICU nurses require a high level of knowledge and skills due to the complexity of the patients. The extended 24-hour stay of the nurses stuff with the patient brings a great deal of responsibility for continuous monitoring of the patient's condition, so in case of deterioration that is reflected in physiological or laboratory changes, the nurse is responsible for identifying this deterioration. However, it can be said that most of the deterioration cases are not detected in time due to lack of knowledge, lack of communication or failure to report (13,14).

The present study aims to examine the nurses' knowledge on HP, RS, and nutrition in general. We analyzed the correlation between the nurses' knowledge on these subjects to rate of HP in their unit, length of ICU stay, duration of mechanical ventilation, and mortality.

**Participants and Methods:**

This study included a convenience sample of 45 ICU nurses. We develop an ICU nurse's questionnaire. The questionnaires were face validated by two nursing master degree students and two nurses from the academic staff in the nursing department at Tel Aviv University, one of whom is an expert in the field. The nurses' were asked rate the questionnaire statements on how much they relate to the variable.

The questionnaire was divided into the following topics :( A) Sociodemographic data that includes 13 items. Items 1-5 relate to socio-demographic characteristics age, gender, country of birth. Items 6-11 refer to professional education, profession, seniority, questionnaire 12-13 relate to education on nutrition.

(B) The nurse's level of knowledge about hypophosphatemia and RS. This section divided to four parts (B1) - Which include 20 statements. Nurses were requested to mark their agreement on the scale 1 = Yes 2 = No and 3 = I do not know. The alpha Cronbach of this section was 0.78, section 1(Questions 1-4) -the level of the nurse's knowledge of his/her role in nutrition (B2)- (Questions 5-7) Knowledge regarding the importance of electrolyte monitoring before feeding the ICU patients. (B3)- (Questions 8-9) Statements examining the nurse's level of knowledge regarding intensive care nutrition (B4) (Questions 10-20) statements examining the nurse's knowledge in general regarding re-feeding syndrome: risk factors, consequences, and treatment.

Lastly, section (C) included 11 items related to what actually happens in the ICU unit. Nurses were requested to rate their agreement with each item on a scale ranging from 1 (never) to 5 (always). The alpha Cronbach of this section was 0.76.

In addition, data collection retrospectively in 2018. The data included an observational study on 275 medical- surgical ICU patients in a tertiary hospital in central Israel. The data was withdrawn from the same unit were the participant nurses were working at. A standard statistical power analysis was performed to determine the size of the study population that would be necessary to demonstrate the study hypothesis (For the model variables other than the nurses' questionnaire). The sample size at a power level of 80% and a significance level of 0.05 was calculated using WinPepi software with the expectation that in patients with hypophosphatemia and RS the intended difference in mortality and complications was lower than 0.05. The patient's data study was collected in the patient data management system (MetaVision; iMDsoft, Tel Aviv, Israel). For each patient, a CRF (Case Report Form) was prepared about the following characteristics: A. demographic data such as age, sex, weight, height and body mass index (BMI). B. Blood laboratory tests at day o,1,2,3,4 of Phosphate (2.5-4.5 mg/dl) Magnesium (1.5-2.00 meq/l), Glucose (70-110 mg/dl), Calcium (8.5-10.9 mg/dl), all of the above tests were performed using the Au, Colorimetric method in the automated device < 2.5

Beckman Coulter, Fullerton, CA, USA (analyzer) Sodium (136-145 mmol/l ) potassium (3.5-5.2 mmol/l) were tested using the ISE method; ion-sensing electrodes indirect method (Beckman-Coulter, Inc., Fullerton, CA, USA). Information about nutrition consumption. D. complication data: mechanical ventilation, length of ICU stay (days), and mortality after 28 days.

The study participants divided into three groups: group A: patients with serum phosphates<2.5 (N=102) during 4 days after receiving nutrition. Group B (N=63) their phosphates level (2.5-4.5) remained normal during four days after initiation. Group C (N=90) with high phosphate level (>4.5) from the ICU hospitalization and four days after initiation, missing data (N=20).

**Results:**

The mean rate of response to the ICU nurses questionnaire was 84%. The results revealed that most ICU nurses are female (64.6%). sixty-two percent of the nurses reported that they had studied a basic course in nutrition as part of their primary nursing studies. Majority of 91.1% thought that nutrition follow-up of the ICU patient is not nurse responsibility. Only 22% think that it is not their duty to perform daily monitoring of electrolytes. However, 75.6% stated that they think there is no significance for monitoring phosphate levels prior to initiation of feeding. More than 64.4% of nurses think that they should start to provide the patient with the full caloric intake immediately after hospitalization in ICU, as opposed to a 35.6% of nurses that believes they should withhold the feeding, as instructed in the latest guidelines(5,15,16).

Sixty eight percent of the nurses are not aware of the increase risk of RS when the patients' level of Phosphate is low. More than half of the nurses (59.1%) do not think that there is a correlation between RS and level of electrolyte (Potassium, Sodium, Calcium, and Magnesium) levels.

In addition, 63.6% think that patients with RS do not need any changes or tuning the maximum amount of calories intake. Sixty two percent of the nurses think that there is no relationships between hypophosphatemia and length of ICU stay and weening from mechanical ventilation. About a third of the nurses (34%) reported that there was no awareness in their department of early detection of RS.

The results show that there is a relationship between the level of knowledge of ICU nurses and behavior in preventing and treating HP and RS. The average of the knowledge test score for all ICU nurses was 61.7%. In the Pearson correlation test, the nurse's knowledge level matches with the medical guidelines and protocol (P <0.05). The results show that as the nurses' knowledge level was higher (rp=0.303, p<0.05), the more the nurses applied according to the current nutrition guidelines. However, there is no difference between a nurse undergoing intensive care and a nurse without a course in intensive care in association with the nurse responsibility for the patient's nutritional status.

Data for ICU patients were collected retrospectively. Patients Mean age was 57±20.3. Mean APACHE II score was 20.4±7.44. On second day after start feeding 45% of the patients with HP significantly lower their phosphate level (Mean = 1.87), which developed into RS . Moreover, after 72 hours, the number of patients with HP was still double (31.4%) compared to the baseline (15%). About one-third (157) of the patients with normal phosphate level developed HP after 24 hours of feeding. In addition, 40% of these patients remained with a low phosphate level after two days, and about a quarter (22%) of them remained with a low phosphate level after 72 hours (Figure 5). These patients also have abnormal additional electrolyte such as Potassium, Sodium, Calcium, and Magnesium, compared with patients with normal phosphate.

From the HP group, 67% of patients developed RS and received dietary intake higher in 50% of the recommended intake. However, in the Kramer correlation test, no significant correlation were found between high caloric intake and development of RS in hypophosphatemia patients and in the normal phosphate groups.

In T- Test for independent samples, a significant difference was found (p <0.006) in the number of length of ICU hospitalization between the groups. Patients with HP and RS with caloric intake greater than 50% of the recommended intake were more likely to be hospitalized in the ICU with mean of 14±9.9 days compare to patients in the same group who received lower caloric intake than 50% of the recommended daily intake (mean 10±7.5 days (p <0.006)).

In addition, in the HP and RS group a significant difference was found in numbers of mechanical ventilation days in the maximum caloric intake with mean of 14±10.1 days compare to the reduce caloric intake group with the mean of 8±7.3 days (p <0.015). No significant difference in mortality rate between the low and normal phosphate level patients, however, the Kramer test found that patients with high phosphate levels (57.8%) had significant high mortality rate (p <0.002 Kramer test 0.219), compared with patients with normal phosphate levels (35.3%).

**Discussion**

The present study goal is to examine the correlation between the nurses' level of knowledge on HP, RF and nutrition, to the patients' outcomes. Overall, the present study shows there is a direct influence of the nurses' knowledge to the patients' complications that resulted from HP and/or RF.

The present study results show that the vast majority (91.1%) of nurses believe that nutrition follow-up of the ICU patient is not their responsibility. Nutrition is interdisciplinary process(17). Nutrition is one of thirteen domain in nursing practice (18). However, from 1950-1970 the nursing role in nutrition separate into two disciplines profession nursing and dietitian (19). from than the nurses responsibility and involvement in patients nutrition therapy has largely been relegated to ancillary staff (20) . These results are supported by the results obtained in the present study. Effective nutrition therapy should include collaboration between medicine, nursing, dietitian and other health care profession. In many institutions, malnutrition managed with isolation in responsibility provided mainly by the dietitian(17) . In spite, the activities of taking in nutrition therapy by nurses the role of the nurse in nutrition is not clearly defined(21).

The present study results show that most of nurses (75.6%) consider monitoring phosphate levels, prior to initiation of feeding, is not significant. In fact, many (64.4%) of nurses believe that they should start to provide the patient with the full caloric intake immediately after admission to the ICU. According to the results of the data collected from the ICU patients, the majority of the patients that received more than 50% of the recommended caloric intake developed complications and RS. From the current results, it is clear why ICU nurses do not update the new guidelines in nutrition. The nutrition education for nurses include basic knowledge. There is no obliged educational hours in basic nutrition for Bachelor of Science in nursing programs. Moreover, no strategies for implementing and continuing nutrition education and what is the role and responsibility of nurses in nutrition(20). According to a study by Stotts et al (22), only 50% of the nurse's students feel satisfied with their nutrition studies.

Additional results of the current study reveal that majority of the nurses are not aware of the increase risk of RS when the patients' level of Phosphate is low. According to the ICU patients' results, on second day after start feeding 45% of the patients with HP significantly lower their phosphate level, which developed into RS and after 72 hours the number of patients with HP double. As mentioned above, hypophosphatemia is the indication of RS(23). Marik et al.(7) Show in prospective study of ICU patient's shows that 34% of patients were diagnosed with RS, and all of those patients had additional decrease of phosphate levels during their ICU stay.

Other metabolic irregularity blood tests are observed, in the present study results, and defines as part of RS include hypokalemia, hypomagnesaemia, and hypocalcemia these results are similar to other studies (3,24,25) Nonetheless, the present study results shows that more than half of the nurses do not think that there is a correlation between RS and level of electrolyte levels.

In addition, the present study results show 63.6% think that patients with RS do not need any changes or tuning the maximum amount of calories intake. zaki et al(3) shows that around third of the patients that start artificial nutrition developed refeeding hypophosphatemia. Moreover, Doig et al(10) shows in randomized control trial that restricted caloric intake compare to normal caloric intake in RS critically ill patients significantly reduce complication and mortality rate in ICU. According to the guidelines for ICU patients at nutritional risk healthcare team should monitor their phosphate and electrolyte, correction fluid insufficiency, thiamine additive and also the healthcare team should restrict their feeding(5,15,16). In the current study, results shown no increase of mortality rate in the RH groups. These results are similar to the results obtained in a study by Zeki et al (3). Which concluded that these results are because there is already many co-morbidities that can cause death in ICU patients, therefore it is hard to distinguish the cause.

The results demonstrate that there is a lack of knowledge on the relationships between hypophosphatemia and patients' outcomes. Nurses stated that there is no correlation between HP and length of ICU stay and weening from mechanical ventilation. In prospective cohort study conduct by Alsumarain et al. (26) on 66 ICU ventilated patients the results show there is an association between hypophosphatemia and failure-to-wean from mechanical ventilation. HP and other electrolyte deviation.

Can cause respiratory failure some study provide explanation of each metabolic discombobulation to failure from mechanical ventilation(27) . In study, demonstrate by Coşkun et al(28). refeeding hypophosphatemia found in 52.14% from 117 ICU patients. The mortality rate was higher and ICU length of stay was longer in the patients with refeeding hypophosphatemia.

The results show that there is a relationship between the level of knowledge of ICU nurses and behavior in preventing and treating HP and RS. The results show that as the nurses' knowledge level was higher, the more the nurses applied according to the current nutrition guidelines. Up to date, the role of nurses in nutrition is suboptimal. Many factors affecting nurses' nutrition therapy knowledge and responsivity in the ICU, including lack of nutrition education, lack of interprofessional collaborative practice, interprofessional team based care etc (29). Studies(30,31) examining ICU patients nutrition therapy for a period of time, show that most of the ICU patients are underfed during their ICU stay. Nutritional treatment start quite slow and not in any way reaches the fulfilled caloric targets. The results of the present study demonstrate that there is a direct effect of the nurses' knowledge to their following current nutrition guidelines, which eventually will improve outcomes. These results indicate that if the nurses received more education, and have positive attitude towards nutrition, it may reduce the incidence of malnutrition in ICU and hospitals. In light of the above, we need develop an interprofessional approach to implementations nutrition therapy to improve quality of care in ICU patients.

In conclusion, the present study demonstrate the importance of monitoring the patients levels of phosphate and treating them accordingly. HP and RS can result in more complications such as length of hospitalization and length of mechanical ventilation. In addition, there is correlation between the level of nurses' knowledge and there approach toward current nutrition guidelines, the higher the nurses' knowledge, the more he/she will follow the current nutrition guidelines. This can be crucial to patients' outcomes and ultimately save the patients life. Therefore, it is essential to educate the nurses more on their role of ICU nutrition.

**Limitations**

Our convenience sample might be unique in their perceptions of a topic, since all participants were selected from the same ICU. Additionally, the accuracy of the questionnaire could be adversely affected by the nurses' high workload that limited there time to answer the questionnaire. A further issue concerns is that the patients' data was collected retrospectively, and there is no certainty that the same nurses that participated in the study treated these patients, though the patients were admitted to the same unit as the participating nurses.

**Bibliography**

1. Lee JW. Fluid and electrolyte disturbances in critically ill patients. Electrolyte Blood Press. 2010 Dec 31;8(2):72–81.

2. Friedli N, Stanga Z, Sobotka L, Culkin A, Kondrup J, Laviano A, et al. Revisiting the refeeding syndrome: Results of a systematic review. Nutrition. 2017 Mar;35:151–160.

3. Zeki S, Culkin A, Gabe SM, Nightingale JM. Refeeding hypophosphataemia is more common in enteral than parenteral feeding in adult in patients. Clin Nutr. 2011 Jun;30(3):365–368.

4. Olthof LE, Koekkoek WACK, van Setten C, Kars JCN, van Blokland D, van Zanten ARH. Impact of caloric intake in critically ill patients with, and without, refeeding syndrome: A retrospective study. Clin Nutr. 2018;37(5):1609–1617.

5. Berger MM, Reintam-Blaser A, Calder PC, Casaer M, Hiesmayr MJ, Mayer K, et al. Monitoring nutrition in the ICU. Clin Nutr. 2019 Apr;38(2):584–593.

6. Crook MA. Refeeding syndrome: problems with definition and management. Nutrition. 2014 Dec;30(11-12):1448–1455.

7. Marik PE, Bedigian MK. Refeeding hypophosphatemia in critically ill patients in an intensive care unit. A prospective study. Arch Surg. 1996 Oct;131(10):1043–1047.

8. Skipper A. Refeeding syndrome or refeeding hypophosphatemia: a systematic review of cases. Nutr Clin Pract. 2012 Feb;27(1):34–40.

9. Friedli N, Stanga Z, Culkin A, Crook M, Laviano A, Sobotka L, et al. Management and prevention of refeeding syndrome in medical inpatients: An evidence-based and consensus-supported algorithm. Nutrition. 2018;47:13–20.

10. Doig GS, Simpson F, Bellomo R, Heighes PT, Sweetman EA, Chesher D, et al. Intravenous amino acid therapy for kidney function in critically ill patients: a randomized controlled trial. Intensive Care Med. 2015 Jul;41(7):1197–1208.

11. Lobo DN. Fluid, electrolytes and nutrition: physiological and clinical aspects. Proc Nutr Soc. 2004 Aug;63(3):453–466.

12. Tagney J, Haines C. Using evidence-based practice to address gaps in nursing knowledge. Br J Nurs. 2009;18(8):484–489.

13. Liaw SY, Scherpbier A, Klainin-Yobas P, Rethans JJ. A review of educational strategies to improve nurses’ roles in recognizing and responding to deteriorating patients. Int Nurs Rev. 2011 Sep;58(3):296–303.

14. Rischbieth A. Matching nurse skill with patient acuity in the intensive care units: a risk management mandate. J Nurs Manag. 2006 Jul;14(5):397–404.

15. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (SCCM) and american society for parenteral and enteral nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2016 Feb;40(2):159–211.

16. Introduction to the 2018 ESPEN guidelines on clinical nutrition in the intensive care unit: food for thought and valuable directives for clinicians!. Current Opinion in Clinical Nutrition & Metabolic Care. 2019;22(2).

17. Tappenden KA, Quatrara B, Parkhurst ML, Malone AM, Fanjiang G, Ziegler TR. Critical role of nutrition in improving quality of care: an interdisciplinary call to action to address adult hospital malnutrition. JPEN J Parenter Enteral Nutr. 2013 Jul;37(4):482–497.

18. Herdman TH. Nursing diagnoses 2012-14: definitions and classification. John Wiley & Sons; 2012.

19. Nightingale F. 1860, Notes on Nursing: What it is and what it is not. 1969;

20. DiMaria-Ghalili RA, Mirtallo JM, Tobin BW, Hark L, Van Horn L, Palmer CA. Challenges and opportunities for nutrition education and training in the health care professions: intraprofessional and interprofessional call to action. Am J Clin Nutr. 2014 May;99(5 Suppl):1184S–93S.

21. Jordan S, Snow D, Hayes C, Williams A. Introducing a nutrition screening tool: an exploratory study in a district general hospital. J Adv Nurs. 2003 Oct;44(1):12–23.

22. Stotts NA, Englert D, Crocker KS, Bennum NW, Hoppe M. Nutrition education in schools of nursing in the United States. Part 2: The status of nutrition education in schools of nursing. JPEN J Parenter Enteral Nutr. 1987 Aug;11(4):406–411.

23. Marinella MA. The refeeding syndrome and hypophosphatemia. Nutr Rev. 2003 Sep;61(9):320–323.

24. Weinsier RL, Krumdieck CL. Death resulting from overzealous total parenteral nutrition: the refeeding syndrome revisited. Am J Clin Nutr. 1981 Mar;34(3):393–399.

25. Miller SJ. Death resulting from overzealous total parenteral nutrition: the refeeding syndrome revisited. Nutr Clin Pract. 2008 May;23(2):166–171.

26. Alsumrain MH, Jawad SA, Imran NB, Riar S, DeBari VA, Adelman M. Association of hypophosphatemia with failure-to-wean from mechanical ventilation. Ann Clin Lab Sci. 2010;40(2):144–148.

27. Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. Eur Respir J. 2007 May 1;29(5):1033–1056.

28. Coşkun R, Gündoğan K, Baldane S, Güven M, Sungur M. Refeeding hypophosphatemia: a potentially fatal danger in the intensive care unit. Turk J Med Sci. 2014;44(3):369–374.

29. Marshall AP, Cahill NE, Gramlich L, MacDonald G, Alberda C, Heyland DK. Optimizing nutrition in intensive care units: empowering critical care nurses to be effective agents of change. Am J Crit Care. 2012 May;21(3):186–194.

30. Heyland DK, Schroter-Noppe D, Drover JW, Jain M, Keefe L, Dhaliwal R, et al. Nutrition support in the critical care setting: current practice in canadian ICUs--opportunities for improvement? JPEN J Parenter Enteral Nutr. 2003 Feb;27(1):74–83.

31. Bendavid I, Singer P, Theilla M, Themessl-Huber M, Sulz I, Mouhieddine M, et al. NutritionDay ICU: A 7 year worldwide prevalence study of nutrition practice in intensive care. Clin Nutr. 2017;36(4):1122–1129.