Comparison of Ramadhan and Pre-Ramadhan Diabetic Ketoacidosis (DKA) Admission Among Type-II Diabetic Mellitus Patients Admitted in Hospital Sultanah Nur Zahirah Kuala Terengganu: Associated Factors, Outcome and Severity.

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LIST OF ABBREVIATIONS

DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
HHS	Hyperosmolar Hyperglycemic State
HSNZ	Hospital Sultanah Nur Zahirah
NMRR	National Medical Research Register
SMBG	Self-monitoring Blood Glucose
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus

ABSTRAK (BAHASA MELAYU)

Pengenalan: Diabetik ketoasidosis (DKA) adalah salah satu daripada komplikasi penyakit diabetis yang membahayakan nyawa. Kajian tentang DKA dalam kalangan pesakit Kencing Manis Jenis 2 semasa Ramadhan adalah terhad di Malaysia terutamanya di kawasan pantai timur. Oleh itu, tujuan utama kajian ini adalah untuk menentukan faktor-faktor berkaitan dengan DKA dalam kalangan pesakit Kencing Manis Jenis 2, dan juga untuk membandingkan tempoh tinggal di hospital, kematian dan tahap keterukan DKA.

Kaedah: Kajian ini merupakan kajian kerat rentas perbandingan. Responden terdiri daripada semua kemasukan DKA dalam kalangan pesakit Kencing Manis Jenis 2 sebelum dan semasa Ramadhan ke wad perubatan di Hospital Sultanah Nur Zahirah, Terengganu di antara Januari 2015 hingga Disember 2019. Data demografik, sejarah dan data klinikal diambil dari rekod perubatan pesakit.

Keputusan: Seramai 177 kes DKA yang telah dimasukkan ke HSNZ, dengan 83 kemasukan adalah sebelum Ramadhan, dan 34 kemasukan adalah semasa Ramadhan. Analisis menunjukkan bahawa penggunaan insulin, serta komplikasi kencing manis merupakan faktor-faktor berkaitan dengan DKA. Selain itu, tiada perbezaan signifikan untuk tempoh di dalam hospital dan kematian di antara sebelum Ramadhan dan semasa Ramadhan ($p>0.05$), manakala tahap keterukan DKA adalah berbeza diantara dua tempoh tersebut ($p<0.001$).

Kesimpulan: Insulin dan komplikasi diabetis merupakan faktor-faktor berkaitan dengan DKA. Tahap keterukan DKA dalam kalangan pesakit Kencing Manis Jenis 2 adalah parah semasa Ramadhan berbanding bukan Ramadhan. Manakala, hasil dan faktor yang menyebabkan DKA adalah sama sebelum dan selepas Ramadhan.

ABSTRACT

Background: Diabetic Ketoacidosis (DKA) is one of the most common life-threatening complications of diabetes mellitus. There are limited published studies on DKA among Type 2 Diabetes Mellitus (T2DM) patients during Ramadhan in Malaysia, particularly in the oast region. Therefore, this study aims to determine the associated factors for DKA admission for T2DM patients, as well as to compare the outcomes and severity of DKA admission between pre-Ramadhan and during Ramadhan.

Method: This is a comparative cross-sectional study. The study population involved all DKA admissions in patients with type 2 DM before and during Ramadhan to medical ward in Hospital Sultanah Nur Zahirah, Terengganu between January 2015 to December 2019. The demographics, underlying history and clinical data for patients were retrieved from the medical records of the patients.

Result: A total of 117 DKA admissions in the medical ward department of HSNZ which involved 83 admissions pre-Ramadhan, and 34 admissions during Ramadhan. Analysis showed insulin and diabetes complications were the associated factors for DKA. Besides, there were no significant differences in length of stay and mortality between Pre-Ramadhan and during Ramadhan ($p>0.05$), whereas the severity of DKA was significantly different between those two periods ($p<0.001$)

Conclusion: Insulin and complications were the associated factors for DKA. The severity of DKA admission in T2DM patients was found to be severe during Ramadhan compared to non-Ramadhan. However, the outcome and factors that lead to DKA admissions was similar during Ramadhan and pre-Ramadhan.

CHAPTER 1: INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia, and accompanied by greater or lesser impairment in the metabolism of carbohydrates, lipids and protein (Baynest, 2015). A survey from National Health and Morbidity Survey (NHMS) in Malaysia discovered that the prevalence of DM in Terengganu had increased by approximately 3.9% from 18.6% in 2015 to 22.5% in 2019 (IPH, 2019).

Diabetic ketoacidosis (DKA) is one of the most common life-threatening acute hyperglycemic complications of diabetes which is usually associated with the absence of effective treatment, coma, stupor and death (Mayer-Davis et al., 2018). It is characterized by the presence of uncontrolled hyperglycemia, metabolic acidosis and increased total body ketone concentration. It had been identified as the most serious acute complication of diabetes (Bedaso et al., 2019). DKA is one of the hyperglycemic emergencies that caused high morbidity and mortality among diabetes patients.

T1DM patients had higher risks of developing DKA than T2DM patients (Getie et al., 2021). The possible explanation is that T1DM patients had insulin deficiency which causes the breakdown of lipids leading to the development of DKA, while T2DM patients had endogenous insulin that prevents lipolysis which eventually prevents the development of DKA. (Getie et al., 2021). In contrast, previous studies in Malaysia found that DKA was associated with T2DM which means that T2DM patients were more prone to DKA than T1DM patients (Huri, Foong, Pendek, & Widodo, 2009; Usman et al., 2015).

Meanwhile, Ramadhan is the fasting month for Muslim people throughout the world. During Ramadhan, they must refrain from taking any foods and drinks from dawn until sunset. Diabetes mellitus patients are exposed to the complications associated with fasting such as hypoglycemia, hyperglycemia, ketoacidosis, hydration and thrombosis (Badshah et al., 2018). The risk of DKA was assumed to be increased during Ramadhan as fasting can cause hypo-insulinemia and hyperglucagonemia, ketones body formation and eventually the development of DKA (Ahmad et al., 2012; Badshah et al., 2018). Diabetic patients that had moderate to severe hyperglycemia with average blood glucose 150-300 mg/dl before fast, advanced microvascular and macrovascular complications, renal insufficiency and had other comorbidities are at high risk for developing DKA during Ramadhan (Ahmad et al., 2012).

The associated factors for DKA admission during Ramadhan include non-compliance to medications (Abdelgadir et al., 2016), frequency of DKA admissions over the preceding 6 months, missed insulin dose and infections (Abdelgadir et al., 2015; Elmehdawi et al., 2009). Previous study in the United Arab Emirates reported that the duration of hospitalization was longer in Ramadhan compared to non-Ramadhan (Abdelgadir et al., 2015), which is contradict to Benghazi-Libya study as they reported duration of hospitalization was similar between Ramadhan and non-Ramadhan (Elmehdawi et al., 2009). Meanwhile, the Saudi Arabian study showed that the duration of hospitalization was significantly higher during Ramadhan compared to Sya'aban, but significantly lower than Syawal (Alshahrani & Alraddadi, 2022). Despite not statistically significant, mortality caused by DKA during Ramadhan was more severe than non-Ramadhan (Elmehdawi et al., 2009).

There are limited studies on DKA among T2DM during Ramadhan in Malaysia, particularly in Terengganu, Malaysia. Therefore, this study aimed to determine the associated factors for DKA admission among T2DM patients, as well as to compare the outcomes and severity between pre-Ramadhan and during Ramadhan.

CHAPTER 2: OBJECTIVE OF THE STUDY

OBJECTIVE OF THE STUDY

2.1 GENERAL OBJECTIVE

To compare associated factors, outcomes and severity of DKA admission before and during Ramadhan in Hospital Sultanah Nur Zahirah, Terengganu.

2.2 SPECIFIC OBJECTIVE

1. To determine associated factors for DKA admission in type 2 DM among patients admitted before and patients admitted during Ramadhan in HSNZ.
2. To compare outcome of DKA admission (mortality and duration of hospitalizations) among patients with type 2 DM patients before and during Ramadhan in HSNZ.
3. To compare the severity of DKA admission among patients type 2 DM admitted before and during Ramadhan in HSNZ.

CHAPTER 3: MANUSCRIPT

JOURNAL: Malaysian Journal of Medical Sciences

TITLE: Comparison of Ramadhan and Pre-Ramadhan Diabetic Ketoacidosis (DKA) Admission Among type-II Diabetic Mellitus Patient Admitted in Hospital Sultanah Nur Zahirah Kuala Terengganu: Associated Factors, Outcome and Severity

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3.1 ABSTRACT

ABSTRACT

Background: Diabetic Ketoacidosis (DKA) is one of the most common life-threatening complications of diabetes mellitus. There are limited published studies on DKA among T2DM during Ramadhan in Malaysia, particularly in the east coast region. Therefore, this study aims to determine the associated factors for DKA admission for T2DM patients, as well as to compare the outcomes and severity of DKA admission between pre-Ramadhan and during Ramadhan.

Method: This is a comparative cross-sectional study. The study population involved all DKA admissions in patients with type 2 DM before and during Ramadhan to medical ward in Hospital Sultanah Nur Zahirah, Terengganu between January 2015 to December 2019. The demographics, underlying history and clinical data for patients were retrieved from the medical record of the patients.

Result: A total of 117 DKA admissions in the medical ward department of HSNZ which involved 83 admissions pre-Ramadhan, and 34 admissions during Ramadhan. Analysis showed insulin and complications were the associated factors for DKA. Besides, there were no significant differences in length of stay and mortality between Pre-Ramadhan and during Ramadhan ($p>0.05$), whereas the severity of DKA were significantly different between those two periods ($p<0.001$)

Conclusion: Diabetes medication and complications were the associated factors for DKA. DKA admission in T2DM patients was found to be more severe during Ramadhan compared to the non-Ramadhan period. However, the outcome of DKA admissions was similar during Ramadhan and pre-Ramadhan.

Keywords: Diabetic Ketoacidosis, Type 2 Diabetes Mellitus, Ramadhan

3.2 INTRODUCTION

DKA is one of the hyperglycemic emergencies that caused high morbidity and mortality among diabetes patients. It is characterized by the presence of uncontrolled hyperglycemia, metabolic acidosis and increased total body ketone concentration. It had been identified as the most serious acute complications of diabetes (1,2). T1DM patients had higher risks of developing DKA than T2DM patients (3). However, previous studies in Malaysia found that DKA was associated with T2DM which means that T2DM patients were more prone to DKA than T1DM patients (4,5).

Diabetic patients with DKA usually experienced fever, abdominal pain, vomiting, polyuria/ polydipsia and nausea (6,7). A study at a public hospital in Northern Malaysia reported that diabetic patients with DKA mostly showed symptoms of nausea, vomiting, dizziness, loss of appetite, fever, lethargy, polyuria/ polydipsia, abdominal pain and shortness of breath (5). The most observed physical sign of those patients were dehydration and Kussmaul breathing (deep and laboured breathing pattern). The study estimated the incidence rate of DKA among multi-ethnic population of Malaysia to be 5.47% (54.7 per 1000 diabetic admissions) (5). Early diagnosis and management of DKA is crucial to improve patient outcomes as it is the most observed hyperglycemic emergency with a high fatality rate (11.3%) in multi-ethnic Malaysian populations (5).

Meanwhile, DKA is one of the major risks associated with fasting during Ramadhan in diabetes patients (8,9). Diabetic patients were considered as very high risk for complications during Ramadhan fasting if he/ she had developed DKA within 3 months before Ramadhan (10). DKA during Ramadhan is thought to be increased because the food intake will be decreased during

the month, which in turn will reduce the insulin dosage (8,9). Prolonged fasting will cause excessive glycogen breakdown and increase both gluconeogenesis and ketogenesis, leading to ketoacidosis (11). Increased risk of DKA incidences might be caused by changes in the timing and dosage of medication during Ramadhan fasting (12). DKA is more common in T1DM, and uncommon in T2DM. One of the biggest studies on DKA during Ramadhan called the EPIDIAR study found an increase in DKA admissions during Ramadhan (13). However, a non-systematic review suggested that fasting during Ramadhan did not increase the risk of DKA (14).

Diabetic patients that had advanced microvascular and macrovascular complications, renal insufficiency, moderate to severe hyperglycemia with average blood glucose 150-300 mg/dl before fast, and had other comorbidities are at high risk for developing DKA during Ramadhan (15). The associated factors for DKA admission during Ramadhan include non-compliance to medications (16), frequency of DKA admissions over the preceding 6 months, missed insulin dose and infections (16,17). In terms of hospital stay, previous study in Saudi Arabia showed that the duration of hospitalization was significantly higher during Ramadhan compared to Sya'aban, but significantly lower than Syawal (18).

There are limited studies on DKA during Ramadhan among T2DM in Malaysia, particularly in Terengganu. Hence, the present study aim is to compare the associated factors and outcomes (length of stay and mortality) as well as the severity of DKA admission before and during the Ramadhan at Hospital Sultanah Nur Zahirah, Terengganu. We hope that this study will provide insight into the prevalence of DKA during Ramadhan in Terengganu. Furthermore, evaluating

the different factors contributing toward DKA in pre-Ramadhan and Ramadhan will help predict patients needing more prioritization in disease monitoring

3.3 METHODOLOGY

Study Population and Study Design

This is a retrospective, comparative study. The study population involved are all DKA admission among T2DM before and during Ramadhan to medical ward in Hospital Sultanah Nur Zahirah, Terengganu from January 2015 to December 2019.

All the data for DKA admission within the period were reviewed and classified. The result of patients who fulfilled the criteria were included in the study. The inclusion criteria were Muslim aged more than 18 years old for both groups, newly diagnosed or pre-existing T2DM, and patient who was admitted for DKA and fasted at least 1 day during Ramadhan. Others were Muslim patients with T2DM admitted for DKA in non-Ramadhan months (Jamadil Akhir, Rejab and Sya'aban).

The exclusion criteria were patients who were admitted for DKA for type 1 DM, gestational diabetes mellitus and patients who did not fast during Ramadhan month. Besides, patients admitted for uncontrolled DM and HHS were also excluded. The data later was divided into 2 main groups: pre-Ramadhan group and Ramadhan group. The study flowchart was illustrated in Figure 1.

Data Collection

The demographics, underlying history and clinical data for patients were retrieved from the medical records of patients who were admitted for DKA at HSNZ from January 2015 to December 2019.

Definitions

a) DKA is defined by hyperglycemia capillary blood glucose >11mmol/L, capillary ketones >3mmol/L or urine ketone ≥2+ and venous pH <7.3 and/or bicarbonate <15mmol/L-base on CPG guideline management of type 2 Diabetes Mellitus 2020
b) Base on the definition from CPG guideline management of type 2 Diabetes Mellitus 2020 -Severe DKA is characterized by venous bicarbonate <5mmol/L, blood ketone >6mmol/L, venous pH < 7.1, hypokalemia on admission <3.5mmol/L, Glascow Coma Scale <12, oxygen saturation <92% on air.
c) Base on the definition from CPG guideline management of type 2 Diabetes Mellitus 2020- Mild DKA is characterize by serum glucose >13mmol/L, serum PH 7.25-7.30, venous bicarbonate 15-18 mmol/L, serum ketone 1+ with anion gap >10, mental status alert,
d) Base on the definition from CPG guideline management of type 2 Diabetes Mellitus 2020-Moderate DKA is characterize by serum glucose >13 mmol/l serum PH 7.0-7.24, venous bicarbonate 10-15 mmol/L, serum ketone 1+ anion gap >12, mental status alert/drowsy
e) Pre-Ramadhan months is defined as 3 months prior to Ramadhan in which patient who were fasted or not fasted 3 months prior to Ramadhan according to Islamic calendar which is Jamadil Akhir, Rejab and Sya'aban

f) DKA admission is defined as numbers of admission for DKA in Ramadhan month and non-Ramadhan months (Jamadil Akhir, Rejab and Sya'aban).

g) Poor glycemic control defined as average fasting blood glucose of >13 mmol/L or HbA1c > 10 %.

Statistical Analysis

The data analysis was performed using IBM Statistic Program for Social Sciences (SPSS version 26.0). All categorical data are presented in frequency and percentage. Meanwhile, numerical data are presented in median and interquartile range (IQR) for non-normally distributed data. Chi-square Test or Fisher's Exact Test was performed to find an association between two categorical variables while Mann-Whitney Test (non-normally distributed data) was used to compare categorical and numerical variables.

Meanwhile, simple and multiple logistic regression will be used to find the associated factors for DKA admission between Pre-Ramadhan and during Ramadhan. $P<0.25$ will be considered as statistically significant.

Sample size calculation

Sample size estimation was calculated by using g-power software (two proportion formula) (Faul et al., 2007). Prior data indicate that the proportion of having infection among DKA in type 2 DM patient during Ramadhan was 0.33 (P0) and the proportion before Ramadhan was 0.48 (P1) (10).

Thus, a minimum sample size of 110 samples per group to be able to reject the null hypothesis with probability (power) 0.8. The type 1 error probability associated with this test of this null hypothesis is 0.05. Pearson's Chi-square test for independence will be used to evaluate this null hypothesis. With an additional of 10% dropout rate, the sample size is 121 sample per group.

With ratio Ramadhan: pre-Ramadhan 1:3, hence the sample size for Ramadhan group was 121 and pre-Ramadhan was 363. Total sample size was 484.

Ethical issue

Ethical approval application was submitted to Jawatankuasa Etika Penyelidikan Manusia (JEPeM), Universiti Sains Malaysia on 9th March 2023 with JEPeM code USM/JEPeM/22120772)

This study approved by National Medical Research Register (NMRR) Malaysia on 22th December 2022 with NMRR ID-22-01995-VVS(IIR)

3.4 RESULTS

Sociodemographic and Baseline Clinical Characteristics

There was a total of 117 DKA admissions included in the analysis. Majority of them were male (56.4%), with a median age of 47 years old. Majority of them were not newly diagnosed (96.6%). In terms of medication, 74.4% of the patients take insulin. Non-insulin in this study means either they take no medication or take oral anti-diabetic (OAD). Most of them had poor compliance (88.0%) and poor blood glucose control (99.1%). Among the DKA admissions,

most of them had moderate severity (49.6%), and only 7.7% died. The sociodemographic and baseline clinical characteristics among the DKA admission are shown in

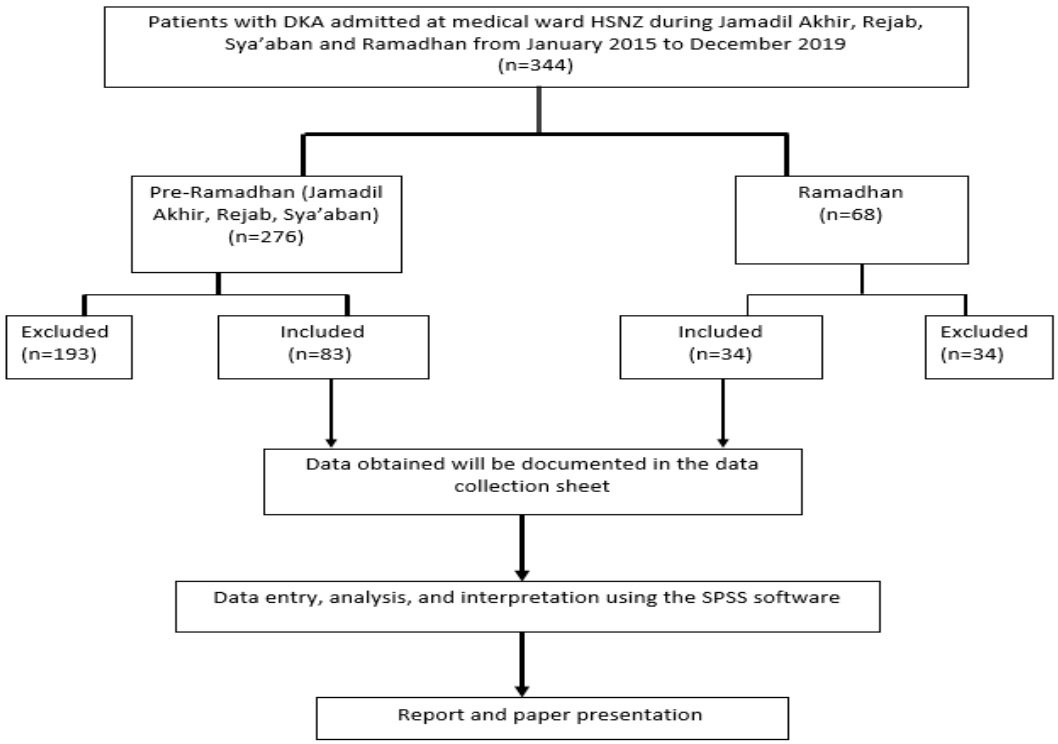

Figure 1: Study flowchart

Table 1.

Associated Factors with DKA Admission

Among the DKA admissions, 83 were pre-Ramadhan, and 34 were during Ramadhan. Two variables were not included in the simple logistic regression, because there was zero count in one of the cells, which lead to analysis error. Nevertheless, simple logistic regression shows several variables had a significant association with the DKA admission, including insulins and complications as shown in Table 2.

In the simple logistic regression, only two variables with $p<0.25$, which were the medication and complication. Thus, for multiple logistic regression variable selection was not done and both variables were fitted in the final models. The final model was tested for multicollinearity and interaction. The final model is shown in Table 3.

DKA Outcomes

When comparing the DKA outcomes between admission pre-Ramadhan and during Ramadhan, there were no significant differences in length of stay and mortality, as shown in Table 4.

DKA Severity

The differences were significant when comparing the severity of DKA between admission pre-Ramadhan and during Ramadhan. Among the pre-Ramadhan admission, the number of admissions with mild, moderate, and severe DKA were approximately similar; however, among the Ramadhan admission, majority of admission were moderate severity. The DKA severity is shown in Table 5.

3.5 DISCUSSION

3.5.1 Associated Factors for DKA among Diabetes Mellitus Patients.

The incidence of DKA among T2DM patients is uncommon (11) as proved by United Arab Emirates (UAE) study since all of their DKA patients during Ramadhan were T1DM patients (19). Similarly, a retrospective study also reported that DKA incidences among T1DM patients are higher compared to T2DM patients during Ramadhan (18). In contrast, a cross-sectional study conducted at 18 public hospitals in Malaysia, namely the DEARS study reported that the majority of DKA admissions were among T2DM patients, whereas the number of DKA admissions was higher during Ramadhan (36.1%) compared pre-Ramadhan (34.5%) and post-

Ramadhan (29.4%) (15). This is the reason why we focused on T2DM patients in the present study.

Prolonged fasting is thought to cause excessive glycogen breakdown, increased gluconeogenesis and ketogenesis which will eventually lead to ketoacidosis and hyperglycemia (8,11). Moreover, prolonged fasting increased the risk of DKA as a result of dehydration which is common during Ramadhan (18). Diabetic patients that fast during Ramadhan are exposed to the risk of DKA and hyperglycemia due to the excessive breakdown of glycogen and increased ketogenesis and gluconeogenesis (11). Changes in meal times, diet patterns as well as changes in timing and dosage of medication during Ramadhan fasting might generate various problems for diabetic patients (12). Therefore, fasting during Ramadhan might be considered as one of the risk factors for DKA (18).

Besides, the DEARS study also reported that gender, age, duration of DM, as well as microvascular and macrovascular complications were not the associated factors for DKA admissions during Ramadhan (20). The present study also found that age and gender of the patients were not statistically different between Ramadhan and pre-Ramadhan. Normally, females and younger ages were associated with an increased risk of developing DKA (21,22). As for Malaysian population, females, adolescents and older adults were more prone to develop DKA (5). Females were more prone to DKA admissions because of the hormonal effects on glucose regulation or because they intentionally avoid good glycemic control with insulin due to fear of weight gain (21).

In this study, we found that insulin as well as complications were the associated factors for DKA occurrence among DM patients before and during Ramadhan which were consistent with the previous studies as they reported that non-compliance and missed insulin dose has been found as factors for increased in DKA incidences during Ramadhan (16,18). The present study also found that patients taking insulin had significantly lower DKA admissions compared to pre-Ramadhan. Previous study had found that diabetic patients on basal bolus insulin regimen had more DKA admission during Ramadhan compared to Syawal, while other insulin regimens including oral hypoglycemic agents and insulin mixtard had lower admission of DKA during Ramadhan compared to Syawal (19), indicating that DKA incidences during Ramadhan fasting can be decreased by changing the insulin regimens or adjusted their dosage (23). From the sub-analysis of our study, most of our patients admitted during Ramadhan were on basal bolus insulin, based on the results from the previous study, we can consider simplifying the insulin regimen in order to improve patients compliances and perhaps to reduce the incidence of DKA during Ramadhan.

Diabetic patients usually decreased their insulin dosage to avoid being hypoglycemic when fasting (5). This is because fasting during Ramadhan increased the risk of hypoglycemia (10). Multiple-dose insulin including short-acting insulin and long-acting basal insulin before meals is recommended for optimum glycemic control and reduced risk of hypoglycemia (10). As example, diabetic patients taking premixed insulin consisting of 70% of intermediate-acting/long-acting insulin and 30% short-acting insulin should change to premixed 50/50 (10). Taking rapid-acting or fast-acting insulin analogues will minimize postprandial hyperglycemia as well as reduce the incidence of hypoglycemia during Ramadhan fasting (12).

In this study, we also found that diabetic-related complications we significantly associated with DKA admission during Ramadhan. Majority of our patients who were admitted for DKA during Ramadhan had both macrovascular and microvascular complications. We do not proceed with logistic regression for each complication to find the association with DKA admission during Ramadhan. Besides, DM patients with renal insufficiency, microvascular or macrovascular complications, moderate to severe hyperglycemia with 150-300 mg/dl average blood glucose before fasting as well as had comorbidities are at risk to develop DKA during Ramadhan (24,15). DKA during Ramadhan can be precipitated by decrease in the dosage of insulin, uncontrolled eating during iftar (meal after sunset), infections, acute stress or illness (10).

Ramadhan-focused diabetic educations must be given to both new and existing DM patients every year prior to Ramadhan, even though existing patients had listened to the same advice during the previous years (20). Nevertheless, diabetic education before Ramadhan is important to control diabetes as well as to increase awareness of the risks related to diabetes (25).

3.5.2 Comparison of Outcome and Severity of DKA before and during Ramadhan.

The present study found that the length of hospitalization was similar during Ramadhan and pre-Ramadhan, which is comparable to the result obtained by the DKAR international study and Benghazi-Libya study (16,17). In contrast, the Saudi Arabia study found that the length of hospital stay was significantly higher during Ramadhan compared to pre-Ramadhan (18). Meanwhile, the DEARS study found that the length of hospital stay was lower during Ramadhan compared to pre-Ramadhan and post-Ramadhan, although no significant difference was observed between those three periods (20). Meanwhile, the Saudi Arabia study reported

that the length of hospitalization was significantly higher during Ramadhan compared to pre-Ramadhan (Sha'aban) (18). They assumed that the longer length of hospitalization during Ramadhan compared to other months was because their most severe cases of DKA were during Ramadhan.

There were no significant differences in mortality between Ramadhan and pre-Ramadhan in the present study which is consistent with the Benghazi-Libya study (17), whereas there was no mortality reported in the DKAR international study (16).

Regarding the severity of DKA, the present study found that most patients who were admitted during Ramadhan month is in moderate-severe as compare to pre-Ramadhan months which show multiple in severity. Meanwhile, the DEARS study found that there are a greater number of diabetic patients with severe DKA during Ramadhan compared to pre-Ramadhan, although they were not statistically different (20). The severity of DKA had a significant impact on the length of hospitalization as reported by the Shanghai study since an increased in severity will increase the duration of hospital stay (26). Similarly, a study in Spain also found that the length of hospital stays was significantly different depending on the severity of DKA (27).

3.6 STRENGTH, LIMITATIONS, RECOMMENDATION AND CONCLUSION.

There are very limited published studies in Malaysia that investigated DKA admissions during Ramadhan. To our knowledge, this is the first study in Malaysia that focused on DKA admissions among T2DM patients, particularly at Terengganu, and therefore can be used as a guide to healthcare professionals regarding the risks of DKA during Ramadhan. The present

study has a few limitations. First, this study only compared before and during Ramadhan. Future studies should also include post-Ramadhan period as previous studies had showed that DKA incidences and length of hospitalization were higher post-Ramadhan (Syawal) (16,18). The second limitation is the retrospective nature of our study. Thus, our result needs to be validated in a prospective study. Another limitation of note is small sample size and single-centre study which focused only on one public hospital located at Terengganu, Malaysia, thus cannot be representative of the DKA for the Malaysian population. a larger sample size may be needed and give a better result.

Overall, insulin as well as complications were the associated factors influencing admission for DKA during Ramadhan and pre-Ramadhan. Furthermore, the severity of the DKA were significantly different between Ramadhan and pre-Ramadhan, while the length of hospital stay and mortality were similar between those two periods. This study highlighted that T2DM patients can fast during Ramadhan safely, as fasting did not increase their risk of developing DKA. Nevertheless, it is crucial for diabetic patients who intend to fast during Ramadhan to undergo pre-Ramadhan education to educate patients on self-management during fasting as well as to educate them on medication adjustment if needed.

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3.8 FIGURES AND TABLES

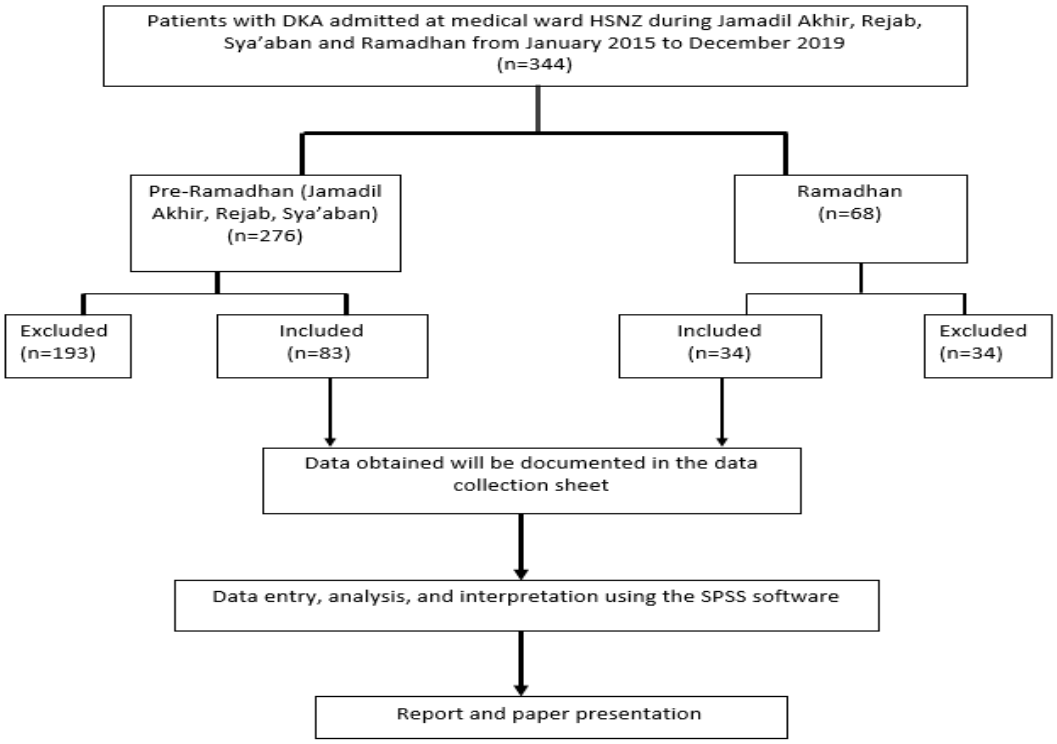

Figure 1: Study flowchart

Table 1: Sociodemographic and Clinical Characteristics among DKA admission (n = 117)

Variables	Overall (n-117) n (%)	Pre-ramadhan (n = 83), n (%)	Ramadhan (n = 34), n (%)	p-value
Gender				0.455[1]
Female	51 (43.6)	38 (45.8)	13 (38.2)	
Male	66 (56.4)	45 (54.2)	21 (61.8)	
Age (years)	47 (34, 57)*	47 (34, 57)*	40 (34, 55)*	0.558[2]
Age (Group)				0.351[1]
18-39	49 (41.9)	32 (38.6)	17 (50.0)	
40-80	68 (58.1)	51 (61.4)	17 (50.0)	
Diagnosis Status				0.999[3]
Known Case of DM	113 (96.6)	80 (96.4)	33 (97.1)	
Newly diagnosed	4 (3.4)	3 (3.6)	1 (2.9)	
Medications				**0.004[1]**
Non-insulin	30 (25.6)	28 (33.7)	2 (5.9)	
Insulins	87 (74.4)	55 (66.3)	32 (94.1)	
Compliance				**0.010[3]**
Non-compliance	103 (88.0)	69 (83.1)	34 (100.0)	
Good Compliance	14 (12.0)	14 (16.9)	0 (0.0)	
HbA1c (%)	12.3 (11.5, 14.0)*	12.4 (11.6, 13.8)*	12.0 (11.0, 14.0)*	0.518[2]
Complications				**0.012[1]**
No Complication	39 (33.3)	34 (41.0)	5 (14.7)	
Complication Present	78 (66.7)	49 (59.0)	29 (85.3)	

[1]Chi-square Test,[2]Mann-whitney U Test, [3]Fisher's Exact Test, *Median (Q1, Q3)

Table 2: Associated factors influencing admission for DKA pre-Ramadhan and during Ramadhan using simple logistic regression (n = 117)

Variables	Crude OR[1]	95% CI	p-value
Gender			
Female (Ref.)			
Male	1.36	0.61, 3.14	0.455
Age (year)	0.99	0.96, 1.02	0.475
Age (Group)			
18-39 (Ref.)			