Case Report:

Nutrition Support for Controlling Blood Glucose in a Case Series of Covid-19 Patients with Hyperglycemia

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INTRODUCTION

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was recognized as a pandemic that has posed a threat to human being global. As of March 2022, the total number of deaths is approximately 6 million people and more than 450 million is the total number of cases worldwide (1).

Mortality and morbidity rates of COVID-19 disease increase significantly in certain population groups such as males, older adults, or patients with comorbidities. Among these, hyperglycemia and diabetes mellitus (DM) have received a lot of attention. Hyperglycemia and DM may be caused by the infection of SARS-CoV-2 to the pancreas through angiotensin-converting enzyme 2 (ACE2), where it is highly expressed compared to other organs, leading to pancreatic damage with subsequent impairment of insulin secretion and development of hyperglycemia even in non-DM patients (2). Apart from that, adipocyte infection and routine steroid treatment could be attributed to insulin resistance and elevated blood glucose (3). Many large studies proved that hyperglycemia and DM may deteriorate the progression and severity of COVID-19 and associate with poorer prognosis and high mortality in suffered patients (4-6). Many studies proved that commercial food suitable for diabetic patients was mostly lower in carbohydrates than the controlling food (7). The use of diabetes-specific nutrition formula (DSNF) has consistently been shown to improve postprandial glucose levels compared to standard test foods such as oatmeal of similar caloric content (8). DSNF could either affect directly through β-cell stimulation and insulin release and/or indirectly through glucagon-like peptide-1 (GLP-1) secretion. In some trials comparing DSNF and standard formula, most DSNF used were oral nutritional supplements (ONS) (8-10). It can be seen that the total carbohydrate mainly ranged from 26 – 31 grams, equivalent to 35-55% total energy, compared to approximately 56 grams of oatmeal (8). A systematic review analyzing 23 different randomized controlled trials showed that DSNF significantly reduced the postprandial rise in blood glucose (by 1.03 mmol/l), peak blood glucose concentration (by 1.59 mmol/l), and glucose area under the curve (by 7.96 mmol) (9). In the ICUs, two different DSNFs outperformed a standard formula in terms of insulin use, plasma glucose, and glycemic variability (11). Because diabetic patients are easily affected and prone to harbor severe symptoms of COVID-19, and because DSNF proved their efficacy in controlling blood glucose as well as other indicators in diabetes, therefore DSNF has been applied more frequently to decrease glucose level, in addition to pharmacological therapy. Besides, in Vietnam, many hospitals use Blenderized Tube Feeding (BTF) foods which makes by kitchen staff with rudimentary technology. Because it has a short expiry date with 24 hours in the fridge, it is not suitable for nourishing the Covid-19 patients during the high peak of the pandemic. In this study, we apply the Nutrition Care Process (NCP) of The Covid-19 Hospital to improve the nutritional condition for those patients and aim to report some cases that consumed a kind of commercial BTF manufactured in Vietnam, which is designed for patients with hyperglycemic. In addition, this product with a reasonable price and a high convenience and therefore become popular in Vietnam during the Covid-19 pandemic.

METHODOLOGY

A case series was conducted at the R13 – Intensive Care Unit at the COVID-19 Hospital which belongs to Hanoi Medical University Hospital. Our clinical study is a case series that includes 10 eligible patients identified during the study registration period (consecutive, formal). It describes the experience of a small group of patients (observational, descriptive research design), contains demographic information about them, 24 hours dietary records, and blood glucose (the lowest and highest blood glucose results each day) during five days consecutive from the initial day to day 5. We collected data on EMR (Electronic Medical Record) on the ISOFH software.

Inclusion Criteria: At admission, patients were diagnosed to have COVID-19 based on PCR testing. All patients had severe COVID-19 infection, which warranted their admission to the hospital. Patients were admitted to the COVID-19 Hospital for at least five days. In addition, the patients were diagnosed with diabetes and presented disorder hyperglycemia with blood glucose above 10 mmol/dl and used nasal tube feeding. All patients received subcutaneous basal-bolus insulin therapy in the hospital for glucose management. Patients were fed by FOMEAL CARE products that specific design for tube-fed patients with high blood glucose.

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Exclusion Criteria: Patients with evidence of a negative for SARS-CoV2 and negative nasopharyngeal smear. Patients had a normal range of blood glucose and did not use tube feeding. In addition, we excluded covid-19 patients who were supported with extracorporeal membrane oxygenation (ECMO), were prone positioning, and had risks of refeeding syndrome.

Data collection: *Nutritional assessment according to GLIM 2018* Assessment nutritional status: we used GLIM 2018 criteria for assessing malnutrition in COVID-19 patients. GLIM 2018 consists of phenotypic criteria (non-volitional weight loss, low body mass index, reduced muscle mass) and etiologic criteria (reduced food intake or assimilation, disease burden/inflammatory condition). (Questionnaire 1)

Body mass index (BMI): We collected the weight and the height of patients through electronic medical records or by asking directly caregivers. BMI category according to WHO classification: BMI < 18.5 Kg/m^2: Underweight; BMI 18.5–24.9 Kg/m^2: Normal weight; BMI 25.0–29.9 Kg/m^2: Pre-obesity; BMI > 30 Kg/m^2: Obesity.

Non-volitional weight loss: we asked patients or caregivers by mobiphone or previous medical staff to know patients' weight loss status.

Reduced muscle mass: nurses or doctors or dietitians would examine or observe some positions on patients' bodies. These are temples, clavicle, shoulder, scapula, thenar, thigh/knee, and calf. In terms of Subcutaneous fat loss, we examine or observe some body's locations such as orbital fat pads, buccal fat pads, and triceps.

Reduced food intake or assimilation: we asked patients or caregivers or previous medical staff to know patients' intake status or we observed patients' eating during the initial 24 hours entering the hospital in the case we could not obtain any information from patients or caregivers or previous medical staffs.

Blood glucose tests: Nurses would check patients' blood glucose before patients' meal time (the main and snack meals) four times a day (6 am; 11 am; 5 pm; 9 pm). All patients had not eaten till nurses examined their blood glucose. They used the ACCU-CHEK Guide machine (Mannheim Germany) for measuring capillary blood glucose for all patients.

Nutrition requirement calculation: Following the ESPEN guidelines on clinical nutrition in the intensive care unit, dietitians calculated nutritional requirements for each patient based on their weight and patients' condition at each phase of the COVID-19 disease. After that, they chose suitable meal codes and/or nutritional products for each participant. The number of patients' meals (3 - 4 meals) would follow patients' nutritional requirements.

+ The patient's meals were provided according to the nutritional intervention plan, the nurse nourished the patient and recorded the number of food intakes each meal. Dietitians would synthesize the 24-hour dietary records. In our research, participants were fed by Fomeal care. Fomeal care is real food that blends meals for diabetes patients or patients with high blood glucose disorder. One portion was packed in a bottle with a net 250ml. The ingredients include macronutrients (14.5 grams protein, 6.6 grams lipid, 25.5 grams carbohydrate), micronutrients (13 vitamins and 12 minerals, and omega 3,6,9. The noticeable characteristics are high fiber content (4 grams per bottle) and low glycemic index (GI = 33±17).

Research implementation

The research was applied the Nutrition Care Process (NCP) of the Nutrition and Dietetic Department at The COVID - 19 Hospital, which include four steps: Nutrition Screening and Assessment, Nutrition Diagnosis according to GLIM 2018 criteria, Nutrition Intervention Plan (nutritional requirements: (protein, lipid, carbohydrate, fiber, meal distribution, and so on), and reassessment a nutritional plan. In our hospital, dietitians would carry out four steps in NCP, nurses would respond to feeding patients through tube-feeding. NST took responsibility for assessment effective nutritional intervention and blood glucose improvement. If patients' blood sugar was unstable and/or insufficient nutrition, the dietitian will change dietary (energy, carbohydrate, and fiber).

Ethics/Consent: The study has been approved by the research review board of Hanoi Medical University Hospital. All participants were fully informed about the purposes of the study.

RESULTS

We presented a case series of 10 patients diagnosed positive with COVID-19 and diabetes mellitus. They were of age group ranging from 67 to 92 years, of which there were five female patients (50%). The study group had a BMI from 19.0 to 27.6 kg/m^2, including two patients with BMI over 25 kg/m^2.

Most of the patients in the study had a severe COVID-19 condition accounted for 80% (8/10 patients), and critical Covid patients were 20% (2/10 patients). All patients had comorbidities, 100% of patients with diabetes mellitus, followed by 50% (5/10 patients) of patients with hypertension and 40% (4/10 patients) of other comorbidities. In addition, seven patients had more than two types of commorbidities. In terms of respiratory therapy, those patients had applied with diversity therapies. Seven patients were supported oxygen by using invasive ventilation (intubation), followed by two patients receiving oxygen masks, and only one patient had non-invasive ventilation (BIPAP).

Table 2 shows that the percentage of patients over 70 years old with BMI < 20 was 30% (3 patients). The percentage of patients with moderate weight loss was 40% (4 patients), which was lower than the proportion of patients without weight loss (60%). Regarding loss of muscle mass characteristics, seven patients did not experience a loss of muscle mass, three patients had a mild to moderate loss of muscle mass, and no patients had a severe weight loss. All patients in our study had a reduction in dietary intake under 50%. Based on GLIM 2018, all patients in our study had a risk of moderate malnutrition at admission.

Table 3 describes the nourishing process of 10 patients during the first five days in the ICU at the

COVID-19 Hospital. For the energy, it reached the recommendation in the first four days. On day 5, the average nourishing energy had a small reduction and achieved 80-99% of the energy requirement. In terms of protein intake, on day 2, day 3, and day 4 of feeding, the average amount of protein in patients' dietary was got to over 95% of the protein requirement. However, on day 1, the average amount of protein among 10 patients' dietary was achieved only 88.8% of this recommendation, and the figure for day 5 was the lowest, at about 76,7%. Besides, the carbohydrate and fiber were completely satisfied with the recommendation. During the research period, the percentage of lipid proportion was not reaching the recommendation ranging from 65% to 74.9 %.

This diagram illustrates the variability of blood glucose and fiber content in the diet of 10 patients during the first 5 days of admission. The highest and lowest blood glucose tended to decrease gradually in the first 5 days. The highest average blood sugar among all participants on day 1 was 21.0 mmol/dL, peaked at 22.1 mmol/dL on day 2, and tended to decrease gradually in the following days. The lowest average blood sugar of 10 patients on day 1 was 8.9 mmol/dL, increased to 12.2 mmol/dL on day 2, and fell to 7.4 mmol/dL on day 5. By contrast, the average amount of dietary fiber showed an upward trend, and it was 14 grams on the beginning day to 18.4 grams on the last study day.

Questtionaire 1.

ASSESSMENT OF NUTRITIONAL STATUS AND REFEEDING SYNDROME

Full name: **Gender:** **Age:** **Weight (kg):** **Height (cm)**
Diagnose

I.Assessment of nutritional status – GLIM 2018		**Level**		
		Normal	Mild- Moderate	Severe
1.Body mass index (BMI)	Mild: BMI >20 if < 70 Age or > 22 if ≥ 70 age	☐		
	Moderate: < 20 if < 70 age or < 22 if ≥ 70 age		☐	
	Moderate: < 18.5 if < 70 age or < 20 if ≥ 70 age			☐
2. Weight loss % (unintended)	Mild	☐		
	Moderate		☐	
	Severe			☐
3. Food intake (Compared to normal)	Mild	☐		
	Reduce <50% of food intake		☐	
	Reduce < 75% of food intake			☐
4. Reduced muscle mass	Mild to moderate	☐		
	Moderate		☐	
	Severe			☐
Classification of malnutrition:		**Classify**		

II. DIANOSTIC CRITERIA FOR THE RISK OF REFEEDING SYNDROME	
High risk of Refeeding Syndrome if patients have a factor below:	Moderate risk of Refeeding Syndrome if patients have two factors below:
☐ BMI: < 16,0 kg/m2	☐ BMI: 16-18.5 kg/m2
☐ Weight loss level: severe	☐ Weight loss level: moderate
☐ Reduced muscle mass/ Subcutaneous fat loss: severe	☐ Reduced muscle mass/ Subcutaneous fat loss: mild to moderate
☐ Reduced caloric intake 75% of total estimated energy requirement	☐ Reduced caloric intake 50% of total estimated energy requirement
☐ Reduced Potassium, Phosphorus ≥ 30%	☐ Reduced Potassium, Phosphorus < 30%

Table 1: Patient characteristics

Patients No.	Gender	Age	Weight (kg)	Height (cm)	BMI (kg/m^2)	Severity of COVID-19 disease	Past medical history	Respiratory therapy
1	Male	74	61	155	25.4	Covid-19 severity	Diabetes, Hypertension	Breathing oxygen through mask
2	Female	80	47.6	148	21.7	Covid-19 severity	Diabetes, Hypertension, Heart failure	Invasive mechanical ventilation (endotracheal)
3	Female	78	55	153	23.5	Covid-19 severity	Diabetes, Hypertension	Breathing oxygen through mask
4	Female	67	65	160	25.4	Covid-19 severity	Diabetes	Invasive mechanical ventilation (endotracheal)
5	Male	76	55	170	19.0	Covid-19 severity	Diabetes, Hypertension	Invasive mechanical ventilation (endotracheal)
6	Female	92	45	152	19.5	Covid-19 severity	Diabetes, Heart failure	Non-invasive ventilation (CPAP or BIPAP)
7	Male	72	65	169	22.8	Covid-19 Critical level	Diabetes, Hypertension	Invasive mechanical ventilation (endotracheal)
8	Male	77	54	168	19.1	Covid-19 Critical level	Diabetes, Heart failure	Invasive mechanical ventilation (endotracheal)
9	Male	90	54.4	161	21.0	Covid-19 severe	Diabetes	Invasive mechanical ventilation (endotracheal)
10	Female	74	78	168	27.6	Covid-19 severe	Diabetes	Invasive mechanical ventilation (endotracheal)

Table 2. Diagnostic Assessment Global Leadership Initiative on Malnutrition (GLIM) 2018

Assessment criteria			Quantity	Percentage
Phenotypic				
1	Low BMI (kg/m^2)	< 18.5 (< 70 years old)	0	0%
		< 20 (>= 70 years old)	3	30%
2	Weight loss	Mild	6	60%
		Moderate	4	40%
		Severe	0	0%
3	Reduced muscle mass	Mild to moderate	7	70%
		Moderate	3	30%
		Severe	0	0%
Etiologic				
1	Food intake	Mild	0	0%
		Reduce <50% of food intake	10	100%
		Reduce < 75% of food intake	0	0%
2	Disease burden/ Inflammatory condition	COVID-19	10	100%

Table 3. The nourishing process of 10 patients in the first 5 days in Intensive Care Unit (ICU)

Nutritional values		Day 1	Day 2	Day 3	Day 4	Day 5
Energy	Energy (kcal) (Mean ± SD)	877± 213	840 ±171	861 ± 184	966 ± 147	1150 ± 147
	Recommended demand- Energy	**870-986 kcal/kg /day (15-20kcal/kg body weight /day)**				**1160-1411 kcal/kg/day (20-25 kcal/kg/ body weight /day)**
	Percentage Recommended demand (%)	Achieve 100% recommended demand				Achieve 80-99% recommended demand
Protein	Protein (grams) (Mean ± SD)	51.5±14.9	58 ±11.8	59.5 ± 12.7	66.7 ± 10.1	66.7 ± 10.1
	Recommended demand - Protein	**58 ± 9.6**	**58 ± 9.6**	**58 ± 9.6**	**69.6 ± 11.5**	**87 ± 14.4**
	Percentage Recommended demand (%)	88.8 %	100%	102.6%	95.8%	76.7%
Lipid	Lipid (grams) (Mean ± SD)	27.7± 6.8	26.4± 5.4	27.1± 5.8	30.4 ± 4.6	30.4± 4.6
	Recommended demand - Lipid	**40.6 ± 6.7**	**40.6 ± 6.7**	**40.6 ± 6.7**	**40.6 ± 6.7**	**40.6 ± 6.7**
	Percentage Recommended demand (%)	68.2%	65%	66.7%	74.9%	74.9%
Carbohydrate	Carbohydrate (grams) (Mean ± SD)	109.2±28.6	102± 20.8	104.5 ± 22.3	117.3 ± 17.8	117.3 ± 17.8
	Recommended demand- Carbohydrate	**Minimum 100-120g/day**				
	Percentage Recommended demand (%)	Achieve 100% recommended demand				
Fiber	Fiber (grams) (Mean ± SD)	14 ± 4.2	16± 3.3	16.4 ± 3.5	18.4 ± 2.8	18.4 ± 2.8
	Recommended demand- Carbohydrate	***14g fiber/1000 kcal***				
	Percentage Recommended demand (%)	Achieve 100% recommended demand				

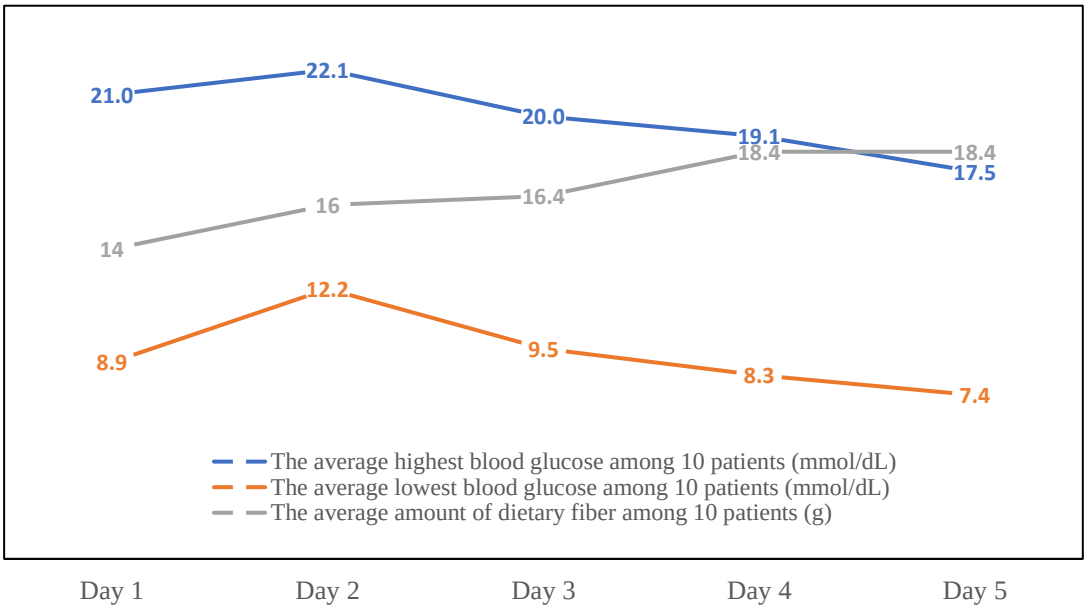

Fig 1. Blood glucose status and dietary fiber content of study subjects for 5 consecutive days

DISCUSSION

The cut-off values of BMI in our study followed the WHO WPRO Asian (12). It can be seen that 4 out of 10 patients have the BMI of overweight and obesity, especially a female patient with a BMI of 27.6. Obesity is a risk factor for severe infection. It has been shown that obesity is associated with worse cytokine storms, the severity, and the longer duration of viral infections (13,14). A retrospective case series conducted in the UK showed that all the patients were overweight or obese (15). Other factors may be related to the fact that obesity may mechanically impair ventilation with reduced aeration of the lung bases that lead to accumulation of secretions and increased risk of infections (16). The patients mainly had comorbidities such as hypertension and heart failure. A case series of 5 patients who suffered from diabetic ketoacidosis, also indicated some common diseases apart from hypertension and congestive heart failure, involving dyslipidemia, end-staged renal diseases, and chronic obstructive pulmonary disease (17). Severe COVID-19 was diagnosed based on Guidelines on diagnosis and treatment the COVID-19 patients - Vietnamese Ministry of Health - 2022 (Breathing beat over 25 or under 10 per minutes; Sp02 < 94% without any oxygen supportive therapies or have to use Non-invasive ventilation (High-flow nasal cannula - HFNC, CPAP, BiPAP) and Invasive mechanical ventilation; the image of lungs on X-ray or CT were hurt more than 50%), which is similar/different to a case series of observations among 8 patients (18).

Hospitalized patients with COVID-19 are at high risk of malnutrition due to an increase in nutritional requirements and a severe acute inflammatory response. All of the candidate patients in our study were recognized as malnutrition, according to GLIM criteria. A retrospective, multicenter study was conducted in 85 diabetic COVID-19 patients from three hospitals in China indicated the prevalence of undernourishment was 41.18% according to NRS-2002. Besides, NRS-2002 and serum pre-albumin were independent predictors of the grade of severity of COVID-19. The malnourished group had more severe illness than the normal nutritional group and had a longer length of in-hospital stay and higher mortality (19). Another retrospective study illustrated similar results, but the prevalence of malnutrition was even higher, at least 60% (20). Of 10 patients, there were 6 cases with mild weight loss and 4 patients with moderate weight loss in our cases report. We did not list which patients had moderate or severe malnutrition to discuss the differences between different ages and severity of malnutrition. Another descriptive, follow-up study used two types of nutritional parameters, BMI and MUST, measured at three different time points (21). According to the Subjective Global Assessment (SGA), 27 out of 75 patients admitted due to a COVID-19 infection had malnutrition. Patients not well nourished were older than patients with an SGA grade A (22). We did not find any research evaluating nutritional state with Global Leadership Initiatives on Malnutrition (GLIM) (23), possibly because GLIM has just been updated and widely published since 2018, therefore there were not many studies using it as a tool.

We followed global guidelines and consensus in terms of nutritional therapy for ICUs patients, which hypocaloric nutrition (not exceeding 70% of energy expenditure) should be prescribed (24). This is based on

the metabolic response to critical illness. In brief, the 'ebb' phase is characterized by hemodynamic instability and hormonal changes (including insulin resistance) in order to prioritize the delivery of energy substrates to vital tissues (25,26). This phase leads to endogenous glucose production as well as lower energy expenditure compared to pre-injury. The 'flow' phase involves the breakdown of tissue to provide substrates to cover the immediate needs for the "fight or flight" response and to reduce the risk of bleeding and infection. The anabolic recovery phase has been described as the resynthesis of lost tissue and the body may be more metabolically able to process delivered nutrients (27,28). Protein acceptted the protein amount delivered by the energy target. After day 3, targeted energy gradually reaches 80-100% measured requirement. Protein target varies by different guidelines, progressively increasing to 1.3g/kg/day (24,25), or expected to be in the range of 1.2 – 2.0 g/kg/day (30). Energy intake of patients in our study achieved 100% energy requirement in the first 4 days in the ICU, but intake in day 5 seemed to be lower than patients' demand, possibly due to the lack of medical workforces during the peak time in Vietnam.

Most study patients were severe and critically ill, therefore their blood glucose seemed high. Our study shows that both the maximum and minimum preprandial glucose experienced a downward trend during the time of using the commercial BTF. In contrast, fiber consumption increased day by day. Some other controlled trials that used similar specialized nutrition formulas also concluded about the reduced glycemic effect of DSNFs (31-33). The low glycemic index of most DSNFs partially contributes to this effect. The commercial BTF with an average GI is 33±17, is a suitable product for diabetes patients. This was not to mention that most of the participants found it easy to tolerate this product during the feeding process. Even so, according to FAO/WHO, the GI of this product is classified as a low GI, therefore it is officially accepted for patients with critical illness, impaired glucose tolerance and/or diabetes. Blood sugar changes after taking this product were significantly lower than those after taking glucose at 15 minutes, 45 minutes, and 60 minutes. Thus, the studied product is safe for diabetic patients because it may gradually increase blood glucose and help to prevent glucose instability and the progress of diabetic complications.

CONCLUSION

Personalize nutritional interventions for patients through the nutritional care process (NCP) for each individual with suitable nutritional products for the patient's condition, which could contribute to improving the nutritional status and blood sugar control for the patient. Dietitians and other medical staff play a key role in taking care of the Covid-19 patients during the pandemic.

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