

Ademolus Hypoglycemic Index

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Abstract

Introduction: This article proposes ADEMOLUS HYPOGLYCEMIC INDEX (AHI) which is a mathematical representation of hypoglycemic episode in a patient with recurrent hypoglycemia over a consecutive three months period.

Methodology: This is a retrospective study of 65 hypoglycemic episodes (HE) occurring in six randomly selected diabetes mellitus patients from 86 case files studied who had attended the endocrinology unit of the Lagos State University Teaching Hospital Ikeja Lagos Nigeria. The data was analysed by using Ademolus Classification of hypoglycemia and the 2018 ADA/EASD Classification of hypoglycaemia to define hypoglycemia. AHI was calculated from the HE using the proposed mathematical formula. SPSS version 23 was used for data analysis.

Results: In all, 65 hypoglycemic episodes occurring in 6 diabetic's patient were studied using ADEMOLUS HYPOGLYCEMIC INDEX. All six patients had a series of hypoglycaemic episodes occurring in three consecutive months. Patient 1 had an AHI of 0.53 using both ACH and ADA/EASD classification.

Discussion: In patient 1 her AHI was not in the severe range. In patient 3, in the last quarter of 2016, her AHI was 0.60, in the first quarter of 2017, her AHI was zero, then between June, July and August 2017 her AHI was 0.64. At this juncture in this patient management, it will be good to evaluate the aetiological factors in this chronic kidney disease diabetic patient who once again has started having recurrent hypoglycemia as it was some six months earlier.

Conclusion: Ademolus Hypoglycemic Index (AHI) is relevant for monitoring of chronic or long term recurrent HE in susceptible individuals.

Keywords: Ademolus Classification of Hypoglycemia; Ademolus Hypoglycemic Index; Hypoglycemia; Diabetes

Abbreviations: AHI: Ademolus Hypoglycemic Index; HE: Hypoglycemic Episodes; ADA: American Diabetes Association; EASD: European Association for the Study of Diabetes; ACH: Ademolus Classification of Hypoglycemia; NPH: Neutral Protamine Hagedom; T1D: Type 1 Diabetes.

CLASSIFICATION OF HYPOGLYCEMIA and ADA/EASD 2018 hypoglycemia classification with significant correlation.

Introduction

The mission of the American Diabetes Association is to prevent and cure diabetes and improve the lives of all people affected by diabetes. The vision is a life free of diabetes and its burdens [1]. However while efforts

Precis

ADEMOLUS HYPOGLYCEMIC INDEX was proposed and used to analyse hypoglycemia using ADEMOLUS

geared towards this is ongoing through intensive research, the iatrogenic complication and burden called hypoglycemia complicating management of the disease is still giving endocrinologist worldwide a challenge to put in mind in the pursuit of glycemic control to clinically desirable value. The interesting thing is that perhaps this challenge of inducing hypoglycemia while trying to achieve euglycaemia perhaps is as old as the management modalities of diabetes mellitus itself dating back to around 460 B.C. to 375 B.C. when Hippocrates was in active clinical practice and even earlier [2]. So it follows that the efforts to limit hypoglycemia complicating diabetes mellitus management has confronted several generations of endocrinologist with yet more grounds to be covered in order to curb morbidity and mortality due to hypoglycemia complicating diabetes management [3-8] whether caused or enhanced by diet, drink, iatrogenic factors or enhanced by co-morbidity [9,10].

The knowledge gap in the area of hypoglycaemia complicating disease condition which has persisted over the years needs to be looked into and addressed by our generation of scientist to move modern healthcare delivery to the next level. It is hoped that as our knowledge improve in this area of hypoglycemia, it will result in better life for people living with diabetes mellitus as a disease. In an effort to curb hypoglycemia complicating diabetes mellitus management and hypoglycemia as a disease entity in general from whatever cause, I hereby propose ADEMOLUS HYPOGLYCEMIC INDEX (AHI) which is a mathematical representation of hypoglycemic episode in a patient with recurrent hypoglycemia over a consecutive three months period. It is as follows;

$$\text{ADEMOLUS HYPOGLYCEMIC INDEX (AHI)} = \frac{\text{Summation of all hypoglycemic episodes for three consecutive months (mg/dl)} \times \frac{1}{100\text{mg/dl}}}{\text{Number of hypoglycemic episodes that occurred within same period}}$$

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

Where:

X= hypoglycemic episodes in three consecutive months in mg/dl

Y= Frequencies of hypoglycemic episodes over same three consecutive months

$$\frac{1}{100\text{mg/dl}} = \text{A Constant}$$

For worldwide use, the standard of measurement is for a span of three consecutive months. ADEMOLUS HYPOGLYCEMIC INDEX is applicable to all disease condition where chronic recurrent hypoglycemia is an

issue [11]. The aim of this original article is to propose ADEMOLUS HYPOGLYCEMIC INDEX (AHI) and to apply it to clinical practice using diabetic patients in order to demonstrate and emphasise its relevance in present day medical practice worldwide.

Methodology

This is a retrospective study of 65 hypoglycemic episodes occurring in six diabetes mellitus patients attending the endocrinology unit of the Lagos State University Teaching Hospital Ikeja Lagos Nigeria. The six patients were randomly selected from 86 case files of diabetic patients studied. Only these six patients had chronic hypoglycaemia occurring in three consecutive months as required in ADEMOLUS HYPOGLYCEMIC INDEX. The second step was that arbitrarily each patient case file was designated as patient 1 to patient 6. The third step was that the data was analysed by using Ademolus Classification of hypoglycemia [12] and the 2018 American Diabetes Association (ADA) / European Association for the Study of Diabetes (EASD) Classification of hypoglycaemia [13] to define hypoglycaemia as 70mg/dl and below, and less than 70mg/dl respectively. The fourth step was that the raw hypoglycaemic values of 70mg/dl and below of each patient 1 to 6 were collected from the case files for three consecutive months using a questionnaire which also extract the frequency of occurrence month by month for corresponding three consecutive months as for the raw hypoglycaemic value, these data is for Ademolus Classification of Hypoglycemia. The fifth step was the raw hypoglycaemic values of less than 70mg/dl and the corresponding frequencies for three consecutive months were extracted using questionnaire these data is for the 2018 American Diabetes Association (ADA) / European Association for the study of Diabetes (EASD) Classification of Hypoglycemia. The sixth step was that Ademolus Hypoglycemic Index was calculated from the hypoglycemic episodes mathematically using the summation of extracted raw hypoglycaemic episodes values over three consecutive months, corresponding frequencies of occurrence over same three months and the constant value 1/100mg/dl as it is obtainable in ADEMOLUS HYPOGLYCEMIC INDEX for Ademolus Classification of Hypoglycemia and for 2018 American Diabetes Association (ADA) / European Association for the study of Diabetes (EASD) Classification of Hypoglycemia respectively. The seventh step is that SPSS version 23 was used to analyse the data further.

The inclusion criteria includes known diabetics patients on treatment whether oral or injectable,

documented history of hypoglycemia (in mg/dl) occurring for 3 consecutive months while on treatment, diabetics with hypoglycemic episodes in the first and third months only of a three consecutive months were included; symptomatic and asymptomatic hypoglycemia were included.

The exclusion criteria include hypoglycemia in non-diabetics, hypoglycemic episodes occurring in two consecutive months with no hypoglycemia in the third month, and diabetics on treatment without any documented hypoglycemic episodes.

Statistical Analysis

By using descriptive statistics, the minimum ADEMOLUS HYPOGLYCEMIC INDEX (AHI) using ADA/EASD classification of hypoglycaemia was 0.46 and it was also 0.46 using ADEMOLUS CLASSIFICATION OF HYPOGLYCEMIA (ACH). By using the two classifications

the maximum of AHI was similar in both classifications with a value of 0.64. The range in both classifications was 0.18, the variance in both classification was 0.003. The standard deviation by using ACH was 0.05380 while by using the ADA/EASD 2018 classification of hypoglycaemia it was 0.5637. The standard error of the mean using ACH was 0.01793 while it was 0.01879 using ADA/EASD 2018 classification of hypoglycaemia.

By using the Pearson correlation statistics, AHI using ADEMOLUS CLASSIFICATION OF HYPOGLYCEMIA correlated well with AHI using 2018 ADA/EASD classification of hypoglycaemia with a value of 0.993. Similarly the findings of AHI derived using ADEMOLUS CLASSIFICATION OF HYPOGLYCEMIA is significant with values derived using ADA/EASD 2018 classification of hypoglycaemia with a p-value of 0.000 (correlation is significant at values of 0.01) (Tables 1 to 5).

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid .46	1	11.1	11.1	11.1
.49	1	11.1	11.1	22.2
.52	1	11.1	11.1	33.3
.53	3	33.3	33.3	66.7
.54	1	11.1	11.1	77.8
.60	1	11.1	11.1	88.9
.64	1	11.1	11.1	100
Total	9	100	100	

Table 1: AHI Using Ademolus Classification of Hypoglycemia.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid .46	1	11.1	11.1	11.1
.49	1	11.1	11.1	22.2
.52	1	11.1	11.1	33.3
.53	4	44.4	44.4	77.8
.60	1	11.1	11.1	88.9
.64	1	11.1	11.1	100
Total	9	100	100	

Table 2: AHI Using 2018 ADA/EASD Classification of Hypoglycemia.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Patent 1	1	11.1	11.1	11.1
Patent 2	1	11.1	11.1	22.2
Patent 3	3	33.3	33.3	55.6
Patent 4	1	11.1	11.1	66.7
Patent 5	1	11.1	11.1	77.8
Patent 6	2	22.2	22.2	100
Total	9	100	100	

Table 3: Frequency of Three Consecutive Months Hypoglycemic Set of Data Values per Patient.

	VAR00001	AHI Using Ademolus Classification Of Hypoglycemia	AHI Using 2018 ADA/EASD Classification Of Hypoglycemia
N Valid	9	9	9
Missing	0	0	0
Std. Error of Mean		.01793	.01879
Std. Deviation		.0538	.05637
Variance		.003	.003
Range		.18	.18
Minimum		.46	.46
Maximum		.64	.64

Table 4: Comparison Of Statistical Analysis Derived From Ademolus Hypoglycemic Index Using Ademolus Classification Of Hypoglycemia And 2018 ADA/EASD Classification Of Hypoglycemia.

		AHI Using Ademolus Classification Of Hypoglycemia	AHI Using 2018 ADA/EASD Classification Of Hypoglycemia
AHI Using Ademolus Classification of Hypoglycemia	Pearson Correlation	1	.993
	Sig. (2-tailed)		.000
	N	9	9
AHI Using 2018 ADA/EASD Classification Of Hypoglycemia	Pearson Correlation	.993**	1
	Sig. (2-tailed)	.000	
	N	9	9

Table 5: Pearson Correlation Of Ademolus Hypoglycemic Index Derived From Both Ademolus Classification Of Hypoglycemia And 2018 ADA/EASD Classification Of Hypoglycemia.

** Correlation is significant at the 0.01 level (2-tailed).

Results

In all, 65 hypoglycemic episodes occurring in 6 diabetes mellitus patient were studied using ADEMOLUS HYPOGLYCEMIC INDEX. The age range was between 19 to 70 years. There were four females and two males. Patient 3 and patient 6 had type 1 diabetes mellitus while the remaining had type 2. All six patients had a series of hypoglycaemic episodes occurring in three consecutive months. Patient 1 had a total of three hypoglycaemic episodes, patient 2 had a total of nine, and patient 3 had a total of eight, patient 4 had a total of sixteen hypoglycaemic episodes, patient 5 had a total of fourteen episodes while patient 6 had a total of fifteen hypoglycaemic episodes. In addition, patient 3 and patient 6 had three and two sets of data respectively consisting of three sets of three consecutive months recording for patient 3 and two sets of three consecutive months recordings for patient 6 (Table 3). By Using Ademolus Classification of Hypoglycemia, Patient 1 had an Ademolus Hypoglycemic Index of 0.53 while patient 2 had a AHI of 0.49. Patient 3 with three sets of three consecutive months data had a AHI of 0.60, 0.64 and 0.53. Patient 4 had a AHI of 0.54 while patient 5 had a AHI of 0.53. Patient 6 with two sets of three consecutive months data had a AHI of 0.52 and 0.46.

By using the ADA/EASD 2018 classification of hypoglycaemia, Patient1 had an AHI of 0.53, patient 2 had a AHI of 0.47. Patient 3 with three sets of three consecutive months readings had an AHI of 0.60, 0.64 and 0.53. Patient 4 had an AHI of 0.53. Patient 5 had an AHI of 0.53 while patient 6 with two sets of three consecutive months readings had an AHI of 0.52 and 0.46. By using the Pearson correlation statistics, AHI using ADEMOLUS CLASSIFICATION OF HYPOGLYCEMIA correlated well with AHI using 2018 ADA/EASD classification of hypoglycaemia with a value of 0.993. Similarly the findings of AHI derived using ADEMOLUS CLASSIFICATION OF HYPOGLYCEMIA is significant with values derived using ADA/EASD 2018 classification of hypoglycaemia with a p-value of 0.000 (correlation is significant at values of 0.01) Tables 1 to 5.

Statistical Analysis of the Six Diabetic Patients Using Ademolus Hypoglycemic Index

The statistical/mathematical calculation is as follows

Patient 1

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

X = hypoglycemic episodes occurring in three consecutive months in mg/dl

Y = Frequencies of hypoglycemic episodes occurring over same three consecutive month

$$AHI = \frac{55+52+53}{3} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{160}{3} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = 53.33 \times \frac{1}{100\text{mg/dl}}$$

$$AHI = 0.53$$

Patient 2

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{(43+55+60+37+42+49+49+70+41) \text{ mg/dl}}{9} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = 49.33 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 0.49$$

Patient 3

In 2016 (October, November and December)

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{(59+61+61) \text{ mg/dl}}{3} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{181 \text{ mg/dl}}{3} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = 60.33 \text{ mg/dl} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = 0.60$$

Patient 3

In 2017 (June, July, August)

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{(67+67+59) \text{ mg/dl}}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = \frac{193\text{mg/dl}}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 64.33 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 0.64$$

Patient 3

In 2018 (May, June, July)

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{51 + 55}{2} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = \frac{106 \text{ mg/dl}}{2} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 53 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 0.53$$

Patient 4

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{62+64+65+45+66+49+38+39+70+56+47+32+55+52+52+69}{16} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 53.81 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$AHI = 0.54$$

Patient 5

$$AHI = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

$$AHI = \frac{(50+50+39+55+62+46+62+57+50+62+61+67+36+50) \text{ mg/dl}}{14} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 53.35 \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.53$$

Patient 6

In 2013 (February, March, April)

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{57+53+65+63+51+59+40+45+37}{9} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 52.22 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.52$$

Patient 6

In 2013 (May, June, July)

$$\text{AHI} = \frac{58 + 41 + 54 + 51 + 42 + 29}{6} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 45.83 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.46$$

Analysis Using ADA/EASD 2018 Classification of Hypoglycemia

Patient 1

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

X = hypoglycemic episodes occurring in three consecutive months in mg/dl

Y = Frequencies of hypoglycemic episodes occurring over same three consecutive month

$$\text{AHI} = \frac{55+52+53}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{160}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 53.33 \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.53$$

Patient 2

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{(43+55+60+37+42 \ 49+49+41) \text{ mg/dl}}{8} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 47 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.47$$

Patient 3

In 2016 (October, November and December)

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{(59+61+61) \text{ mg/dl}}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{181 \text{ mg/dl}}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 60.33 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.60$$

Patient 3

In 2017 (June, July, August)

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{(67+67+59) \text{ mg/dl}}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{193 \text{ mg/dl}}{3} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 64.33 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.64$$

Patient 3

In 2018 (May, June, July)

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{51+55}{2} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{106 \text{ mg/dl}}{2} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 53 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.53$$

Patient 4

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{62+64+65+45+66+49+38+39+56+47+32+55+52+52+69}{15} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 52.73 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.53$$

Patient 5

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{(50+50+39+55+62+46+62+57+50+62+61+67+36+50) \text{ mg/dl}}{14} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 53.35 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.53$$

Patient 6

In 2013 (February, March, April)

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = \frac{57+53+65+63+51+59+40+45+37}{9} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 52.22 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.52$$

Patient 6

In 2013 (May, June, July)

$$\text{AHI} = \frac{58+41+54+51+42+29}{6} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 45.83 \text{ mg/dl} \times \frac{1}{100 \text{ mg/dl}}$$

$$\text{AHI} = 0.46$$

Discussion

The chronicity of hypoglycemic episodes complicating the management of diabetes mellitus especially in type 1 diabetes mellitus cannot be overemphasized [14-16], just as is the chronicity of hyperglycemia which is the hallmark of diabetes mellitus as a disease entity [17-19]. The persistence and reality of these hypoglycemic episodes is more understood or appreciated when continuous glucose monitoring methods is adopted in diabetic patients [20-22].

Interpretation of Ademolus Hypoglycemic Index

Interpretation of Ademolus Hypoglycemic Index is as follows, the lower the value of the Ademolus Hypoglycemic Index the more severe the average or mean of the series of hypoglycemic episodes it connotes/represents over the specified three consecutive month period and the poorer the prognosis and outlook. The higher the Ademolus Hypoglycemic Index, the better the prognosis in the patient. A Ademolus Hypoglycemic Index of zero in a three consecutive months indicate no hypoglycemic index over the same period but this does not equate to no hypoglycemic episodes within the same periods. So if in a quarter a patient had a Ademolus Hypoglycemic Index value but the next quarter the patient does not, then it means the patients hypoglycemic episodes (if they still occurred) is becoming clustered instead of been spread out over three consecutive months

and a reason for this change in distribution and pattern of hypoglycemic episodes should be sort! Generally speaking a Ademolus Hypoglycemic Index of 0.40 or below in diabetics is a pointer to a series of chronic severe hypoglycemic episodes and should trigger in the attending endocrinologist/physician a need to screen for a reversible or irreversible central nervous system damage if this has not been done before now. ADEMOLUS HYPOGLYCEMIC INDEX is not a measure of frequency of hypoglycaemia though it is a function of it and it brings the frequency of hypoglycaemia into consideration while calculating ADEMOLUS HYPOGLYCEMIC INDEX. It follows that it will help physician and patients to notice (while calculating and comparing results of previous AHI with recent one) if the frequency of hypoglycemic episode is reducing, same or increasing over a three consecutive months period!

Clinical Implication of Ademolus Hypoglycemic Index

Neuroglycopenic symptoms is known to be a hallmark of severe hypoglycemia and with very severe hypoglycemia, patients clinical condition can progress to reversible or irreversible neurological damage if persistent due to neuronal metabolic injury. One of the clinical implication of ADEMOLUS HYPOGLYCEMIC INDEX is that the risk of developing reversible or irreversible neurological damage can be reduced clinically as patient with mild to moderate form of chronic hypoglycemia yet to develop irreversible neurological damage or neurological sequelae can be prevented early enough from progressing to such irreversible state since a reduced ADEMOLUS HYPOGLYCEMIC INDEX value out of a series of such values will be a pointer towards progression to neurological damage if it has not occurred! This can be achieved by way of tracking the chronic hypoglycemic episodes in terms of series of absolute value, frequency of occurrence and dispersion over a three consecutive months period and comparing series of ADEMOLUS HYPOGLYCEMIC INDEXES over a six months, nine months and twelve months period. Over a three months period, if the hypoglycemic episodes is concentrated in two consecutive months, that is ADEMOLUS HYPOGLYCEMIC INDEX of zero, it alerts that there is persistent deprivation of glucose to the brain over a relatively short interval of weeks as against if same frequency of hypoglycemia is spread over three months. For those who had developed irreversible neurological sequelae already, further chronic hypoglycemia that will worsen this neurological sequelae of hypoglycemia will be put to check early enough so that there will be a slow progression of the morbidity to mortality from such irreversible neurological deficit! Using ADEMOLUS

HYPOGLYCEMIC EPISODES will also help to improve the quality of life of affected patients in the long run.

Similarly continuous use of ADEMOLUS HYPOGLYCEMIC INDEX will overtime open up new path of scientific knowledge and research into five years and ten years pattern of survival rates in affected individuals with chronic hypoglycaemia especially in disease conditions associated with hypoglycemia like diabetes which runs a chronic course and can last for decades in people living with the disease. Furthermore, the degree of severity of hypoglycaemia chronicity which is what ADEMOLUS HYPOGLYCEMIC INDEX measures can be compared to sequelae of chronic hypoglycemia in a given study population in terms of ethnicity, drug groups for instance different generations of sulphonyurea and so on. Equally disease conditions with hypoglycemia as a chronic feature or complication can be compared objectively in the future for hypoglycemia severity in different settings of healthcare delivery e.g. general wards, intensive care units, high dependency units and so on with the possibility of gaining more scientific insights. This will help to create value for clinical researchers who focus on this new area of research.

Application of Ademolus Hypoglycemic Index

In the six patients illustrated in this article, some salient points are highlighted. In patient 1, a 63 year old diabetic lady with macrovascular complication [23-25], she had bilateral diabetes foot syndrome and had had bilateral amputation as a result, for the three consecutive months, she was on soluble insulin and Neutral Protamine Hagedom (NPH) her Ademolus Hypoglycemic Index was 0-53. It is significant to note that her Ademolus hypoglycemic index is not in the severe range despite the recurrence.

Patient 2 is a 61 year old diabetic on soluble insulin and NPH and metformin, she had quite a number of recurrent hypoglycemic episodes nine in all during the three consecutive months her Ademolus Hypoglycemic Index was 0.49. Patient 3 gave a good illustration of Ademolus Hypoglycemic Index. She is a 62 year old diabetic with stage 3 chronic kidney disease. She was on insulin glargine. In the last quarter of 2016, her Ademolus Hypoglycemic Index was 0.60, in the first quarter of 2017, her Ademolus Hypoglycemic Index was zero (meaning no hypoglycemic episodes spanning the three consecutive months), then between June, July and August 2017 her Ademolus Hypoglycemic Index was noticed to be 0.64. At this juncture in this patient management, it will be good to evaluate the aetiological factors in this chronic kidney disease diabetic patient who once again have started

having recurrent hypoglycemia as it was some six months earlier, could it be dietary, compliance issue or progression of chronic kidney disease by way of falling glomerular filtration rate [26-28] or what? Furthermore in May to July 2018 she had an Ademolus Hypoglycemic Index of 0.53 after an Ademolus Hypoglycemic Index of zero for two consecutive quarters of a year! She needs close evaluation for this finding too! This proves Ademolus Hypoglycemic Index can be clinically revealing in the long term in patients with recurrent hypoglycemic episodes.

Patient 4 had a Ademolus Hypoglycemic Index of 0.54 while patient 5 had a Ademolus Hypoglycemic Index of 0.53. Patient 6 had two consecutive reading of Ademolus Hypoglycemic Index for two consecutive quarter of a year (though not a consecutive quarter of a calendar year). The revealing result is that she is chronically deteriorating gradually and tending towards more severity in her development of hypoglycemic episodes as her Ademolus Hypoglycemic index fell from 0.52 in the preceding quarter to 0.46, this connotes worsening hypoglycemic state over time and a poorer prognosis. The lower the Ademolus Hypoglycemic Index, the poorer the prognosis.

Ademolus Hypoglycemic Index and Hypoglycemic Index

In literature, an attempt had been made to use hypoglycemic index with little success in its application to day to day clinical wellbeing of the diabetic patients, it was defined as the fall in blood glucose level during a 90-minute period before reaching the nadir divided by the value of the glucose nadir and was applied to diabetes mellitus patient [29].

Ademolus Hypoglycemic Index on the other hand is applicable to both diabetic and non-diabetic patients with an easy to use formula for clinical use, its parameters are almost noninvasive to obtain, samples from just a finger prick for glucometer reading is enough, though venipuncture may be employed in some cases where laboratory value of hypoglycemia is desirable. While hypoglycemic index developed about four decades ago is dependent on hyperinsulinaemic state, Ademolus Hypoglycemic Index is dependent on therapeutic agents/modalities employed in the process of trying to induce euglycaemia though the basal insulin status of the patient will play a role. Also Ademolus Hypoglycemic index measures chronicity of hypoglycemia in patients over three consecutive months (90 days) while hypoglycemic index only put hypoglycemia occurring in the acute phase (over 90 minutes) into consideration.

Ademolus Hypoglycemic Index and Endocrine Society Practice Guideline on Management of Diabetes in the Elderly

In a clinical practice guideline released this year 2019 by the Endocrine Society and also co-sponsored by the European Society of Endocrinologist and the Obesity Society (7), it is stated that " In patients aged 65 years and older with diabetes, an endocrinologist or diabetes care specialist should be primarily responsible for diabetes care if the patient has type 1 diabetes (T1D), or requires complex hyperglycemia treatment to achieve treatment goals, or has recurrent severe hypoglycemia, or has multiple diabetes complications". This is a very good clinical practice guideline which is acceptable. However it will be more practicable and objective if the endocrinologist or diabetes care specialist involved in such scenario in the elderly diabetic where there is recurrent severe hypoglycemia uses ADEMOLUS HYPOGLYCEMIC INDEX as a yardstick of measurement to see the pattern of occurrence and recurrence of hypoglycemia over three months, and monitor to see, using the ADEMOLUS HYPOGLYCEMIC INDEX, when the elderly diabetic is coming out of hypoglycemia and how well the patient is coming out of the episodes in the preceding quarter of the year and a subsequent quarter, if the recurrent severe hypoglycemia persist for that long, it will allow for objective monitoring over a long period in the easily prone elderly diabetic [30]. In that scenario too the ADEMOLUS HYPOGLYCEMIC INDEX can be used to prognosticate objectively over the two quarters of the year or more!

Limitation

The limitations of this study include the fact that there is no previous study or data on Ademolus Hypoglycemic index to compare these findings in the present study with since Ademolus Hypoglycemic Index is being proposed for the first time but at the same time this article now serves as a template or reference for future study. The small sample size of diabetics and the small sample size of hypoglycemic episodes involved are other limitations but notwithstanding; scientifically proven deductions were still derivable from the sample size used. The study was carried out in blacks in Africa instead of a multiracial study including whites, Asians Latin Americans etc. this limitations can be overcome by replicating the same study in other races.

Future Direction

Relevant study for future direction in understanding Ademolus Hypoglycemic Index the more should include

establishing the relationship between Ademolus Hypoglycemic index and glycosylated haemoglobin for the same three consecutive months in relation to the type of treatment modality the diabetic patient is on! Could the relationship (if any) be direct or an inverse one mathematically? The effects of Ademolus Hypoglycemic Index on life expectancy and quality of life in newly diagnosed and long standing diabetics and other disease state where hypoglycemia is a major issue like insulinoma etc. is another area to explore scientifically in the near future.

Conclusion

ADEMOLUS HYPOGLYCEMIC INDEX (AHI) is a mathematical representation of hypoglycemic episode in a patient with recurrent hypoglycemia over a consecutive three months period. It is as follows;

ADEMOLUS HYPOGLYCEMIC INDEX=

Summation of all hypoglycemic episodes for 3 consecutive months (mg/dl) $\times \frac{1}{100\text{mg/dl}}$
Number of hypoglycemic episodes that occurred within same period

$$\text{AHI} = \frac{\sum X}{\sum Y} \times \frac{1}{100\text{mg/dl}}$$

Where:

X= hypoglycemic episodes in three consecutive months in mg/dl

Y= frequencies of hypoglycemic episodes over same three consecutive month

$$\frac{1}{100\text{mg/dl}} = \text{A Constant}$$

For worldwide use, the standard of measurement is for a span of three consecutive months. Ademolus Hypoglycemic Index application is diverse worldwide and is applicable to diabetics and non-diabetics. It is relevant for chronic or long term monitoring of recurrent hypoglycemic episodes in susceptible individuals or scenarios. ADEMOLUS HYPOGLYCEMIC INDEX is a step in the right direction towards fulfillment of the mission and vision of the American Diabetes Association which is to prevent and cure diabetes and improves the lives of all people affected by diabetes and to have a life free of diabetes and all its burdens of which hypoglycemia is one!

"The knowledge gap in management of chronic hypoglycemia complicating diabetes mellitus management or chronic hypoglycemia in other disorders which had been there for millenniums and centuries since

the days of Hippocrates is now being filled by ADEMOLUS HYPOGLYCEMIC INDEX!"

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