CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1704212

Available online at: http://www.iajps.com *Research Article*

PREVELANCE OF DAWN PHENOMENON AND SOMOGYI EFFECT IN DIABETIC PATIENTS

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Abstract:

Patient with diabetes mellitus may have morning hyperglycemia despite of management due to somogyi effect and dawn phenomenon. Occurrence of dawn phenomenon is due to relative deficiency of insulin during the night time when insulin antagonist harmones are rising, so patient experience morning hyperglycemia and hypeglycemia at midnight as well. Somogyi effect occurs due to relative insulin excess which causes midnight hypoglycemia and subsequent morning hyperglycemia due to effects of reactionary raised insulin antagonizing harmones. In this study, 41(21%) out of 200 selected diabetic patients were having morning hypoglycemia despite of insulin therapy. 8(19%) were experiencing it due to somogyi effect and remaining 34(81%) due to dawn phenomenon. Strict glycemic control is essential to prevent complications of diabetes mellitus. Hence, these morning hyperglycemic patients must be screened and their insulin regimen adjusted accordingly.

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Please cite this article in press Adnan Sharif et al., ***Prevelance of Dawn Phenomenon and Somogyi Effect in Diabetic Patients.,*** *Indo Am. J. P. Sci, 2018; 05(12).*

INTRODUCTION:

Diabetic patients taking insulin for glycemic control may have morning hyperglycemia. It can be due to two possible reasons: 1. dawn phenomenon 2. Somogyi effect

The dawn phenomenon occurs when endogenous insulin secretion decreases or when the effect of the exogenous insulin administered to the patient at the previous evening disappears, together with a physiological increase in insulin-antagonistic hormones. The dawn phenomenon is more common than the Somogyi effect.

Somogyi effect occurs in a person if he administer more than required insulin or doesn't eat a regular bedtime snack, and the person's blood sugar level drops during the night. As a response to that hypoglycemia the person's bodyresponds by releasing hormones (cortisol, glucagon and growth hormone) that raise the blood sugar level.

Dawn phenomenon

Definition and pathogenesis

Recurring abnormally high plasma glucose levels inthe morning before breakfast are commonly called thedawn phenomenon. According to the daily insulin secretion profile [1], the dawn phenomenon can be divided into two types: physiologicaland pathological. Both types occur at the same time ofthe day but differ in thevalue of plasma glucose levels. The physiological dawnphenomenon is associated with a natural decrease ofinsulin secretion at midnight combinedwith elevation of blood glucose level remaining up tostandard. This decrease of insulin secretion unblocks the secretion of insulin-antagonistic hormones with hyperglycaemi cproperties, particularly GH. The morning plasma glucose level growth in non-diabetic peoplewith undisturbed insulin secretion is compensated byan additional burst of insulin. In turn, diabetic patientsmay experience the pathological dawn phenomenon,where the morning plasma glucose level is abnormallyhigh due to insulin secretion disturbances plus the effects of nocturnal GH secretion [2].

The dawn phenomenon is a combination of an initialdecrease in insulin requirement followed by an increase in the insulin needs [3]. Therefore,the dawn phenomenon can occur among both peoplewith type 1 and type 2 diabetes mellitus with deterioration of beta cells function and without insulin therapy[4–6]. The decrease of endogenous insulin causesthe lack of sufficient repression of insulin antagonistic hormones secretion, mainly GH [7], cortisol and catecholamines [8] and leads to hyperglycaemia. Becauseof the impaired function of pancreatic beta cells, thereis also an insufficient insulin secretion in response tohyperglycaemia which causes long-acting hyperglycaemia, detected by patients after awakening as the dawnphenomenon. Likewise, the dawn phenomenon occurswhen the action of exogenous insulin administeredto the patient the previous day is running out, and atthe same time overlapping physiological growth ofinsulin-antagonistic hormones is observed. There is alsothe phenomenon called 'extended dawn phenomenon' [9]. This is seen when the high morning glucose levelremains high until mid-morning. The cause of extendeddawn phenomenon can be too many carbohydrates inthe breakfast meal, or the pathologically extended stageof growth hormone secretion which is not repressed by hyperglycaemia, seen more often among diabetic patients [10].

The Somogyi effect

Definition and pathogenesis

Although the existence and pathogenesis of the dawnphenomenon are indisputable in scientific society, theSomogyi effect is still a matter of debate. The name of thephenomenon derives from the surname of Austro-Hungarian scientist Michael Somogyi. In 1949, during theACS meeting in Atlantic City, he made a speech aboutinsulin's influence on diabetic patients. On the basis ofhis investigations, he concluded that people who hadbeen given too large doses of insulin became "actuallyvictims of chronic insulin poisoning" [11]. In his paperentitled: "Exacerbation of diabetes by excess insulinaction", Somogyi developed his initial statement byadding a conclusion that too much insulin led throughhypoglycaemia to hyperglycaemia [12]. Moreover, Somogyi created a hypothesis that hyperglycaemia afterhypoglycaemia is a result of the insulin-antagonisticaction of some hormones, especially those belonging tothe hypothalamic-pituitary-adrenal axis [12]. The riskof occurrence of the Somogyi effect is also increased by using NPH insulin in diabetes therapy, which canbe connected with the evident peak of its concentration taking place 4-5 hours after evening injection andits intermediate duration of action (10–16 hours) [13].According to Raskin [14], asymptomatic nocturnal hypoglycaemia is common, but subsequent fasting hyperglycaemia is not necessarily the result of "rebound", because the present therapeutic regimensof NPH/Lente insulin given at suppertime cause over night hyperinsulinaemia. Excessive fasting hyperglycaemia rarely follows nocturnal hypoglycaemia, except when excessive glucose is ingested to correct hypoglycaemia [3]. Moreover,

nocturnal hypoglycaemia correlates with falling plasma insulin levels rather thanwith increasing concentrations of counter regulatory hormones, whose secretion is often disturbed [14]. Suchdeterioration in insulin-antagonistic hormone levels during asymptomatic nocturnal hypoglycaemia was proved by Jones et al. [15] in a group of patients with type 1 diabetes and without diabetes. Among patientswith diabetes, plasma epinephrine and norepinephrine responses to hypoglycaemia were blunted or reducedwhen they were asleep. The patients' plasma cortisolconcentrations did not increase, while GH concentrations increased slightly. This defective glucose counter regulation is associated with substantially increasedrates of severe iatrogenic hypoglycaemia in people with type 1 diabetes [16].

Somogyi's hypothesis has been tested by numerousscientists, who have accepted or rejected its existence. Research supporting the existence of the Somogyi effect includes the experiment carried out by Matyka et al. [17].Their study involved two groups of 29 type 1 diabeticand non-diabetic children. The aim of the study wasto determine the response of insulin-antagonistic hormones to hypoglycaemia. The results revealed a smallincrease of plasma GH and a rise of plasma epinephrineduring nightly hypoglycaemia compared to a night without hypoglycaemia. The levels of norepinephrine,cortisol and glucagon were the same after a night withor without hypoglycaemia. Furthermore, the abovementioned study found a significant increase in plasmainsulin concentration between 11 p.m. and 3 a.m. amongtype 1 diabetic children, but not in non-diabetic children [17]. Perriello et al. [18] showed that fasting andpost-breakfast plasma glucose levels were significantly higher after nocturnal hypoglycaemia than when hypoglycaemia was prevented. Moreover, fasting levelsof plasma glucose in their study correlated directlywith overnight plasma levels of epinephrine, GH andcortisol. Bolli et al. [19] drew similar conclusions, and indicated that hypoglycaemia can cause rebound hyperglycaemia in the absence of insulin waning in patientswith type 1 diabetes, and that this results primarilyfrom an excessive increase in glucose production dueto activation of glucose counter regulatory systems. Inanother study [20], the authors observed the presenceof the relationship between the Somogyi effect and the exuberant counter regulatory release of GH caused bynocturnal hypoglycaemia among patients with type 1diabetes.

Tordjman et al. [21] assessed whether nocturnal hypoglycaemia actually caused morning hyperglycaemia among type 1 diabetic patients. Their results contradictthe existence of the Somogyi effect, as the presence of nightly hypoglycaemia was not followed by the development of morning hyperglycaemia. Moreover, the morning plasma glucose positively correlated with the nocturnal plasma glucose levels. Similar studies, but using CGMS, conducted by Guillod et al. [22] and Høi-Hansen et al. [23], also proved that morning hyperglycaemia was not related to nightly hypoglycaemia. Furthermore, Monnier et al. [24] demonstrated that nocturnal hypoglycaemia resulted in hyperglycaemia the next day, if it was observed before noon, but notin the early morning, which is called 'mid-morning hyperglycaemia'. Somogyi's next hypothesis investigated by scientists was the relationship between morning hyperglycaemia and the levels of hormones with antagonisticaction to insulin as a result of nightly hypoglycaemia. Gale et al. [25] examined two groups of 15 patientswith and without episodes of nocturnal hypoglycaemia for increased plasma level of GH, cortisol andglucagon during the morning hyperglycaemia. Theresults showed no increase in insulin-antagonistichormone levels among patients with hyperglycaemia and a negative correlation between the plasmaglucose concentration and the plasma free insulinconcentration. This proves that during morning hyperglycaemia, a decrease in plasma insulin levels isobserved. This suggests that hyperglycaemia may be the result of insulin dropping late at night, rather thanan increase of insulin-antagonistic hormones. Similarconclusions were drawn also by Fowelin et al. [10] andHirsch et al. [26].According to above-cited data; the existence of the Somogyi effect has not been definitively proven. However, science supposes it to exist, and it is supposed to bepresent in clinical practice among large number of patients with morning hyperglycaemia. With regard to theimpact of the excessive dose of insulin on the Somogyi effect, it is highly probable that this phenomenon canoccur not only among patients with type 1 diabetes, butalso among patients with type 2 and secondary typesof diabetes, provided patients have been intensively treated with insulin the nocturnal plasma glucose levels. Similar studies, but using CGMS, conducted by Guillod et al. [22] and Høi-Hansen et al. [23], also proved that morning hyperglycaemia was not related to nightly hypoglycaemia. Furthermore, Monnier et al. [24] demonstrated that nocturnal hypoglycaemia resulted in hyperglycaemia the next day, if it was observed before noon, but notin the early morning, which is called 'mid-morning hyperglycaemia'. Somogyi's next hypothesis investigated by scientists was the relationship between morning

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Objective of Study

This study was aimed at finding the prevalence of morning hyperglycemia in diabetic patients who were already on insulin therapy and categorize them between dawn phenomenon and somogyi effect.

Study Design

Cross sectional study

Sampling Size: 200 patients

Sampling Technique: Patients were selected by convenient sampling (simple random sampling)

Inclusion Criteria: Known diabetic patients of all age groups taking insulin therapy (atleast from 1 month).

Exclusion Criteria: Diabetic patients on oral hypoglycemic.

Place and Duration: This study was conducted in North Medical Ward Mayo Hospital Lahore from May 2018 to July 2018

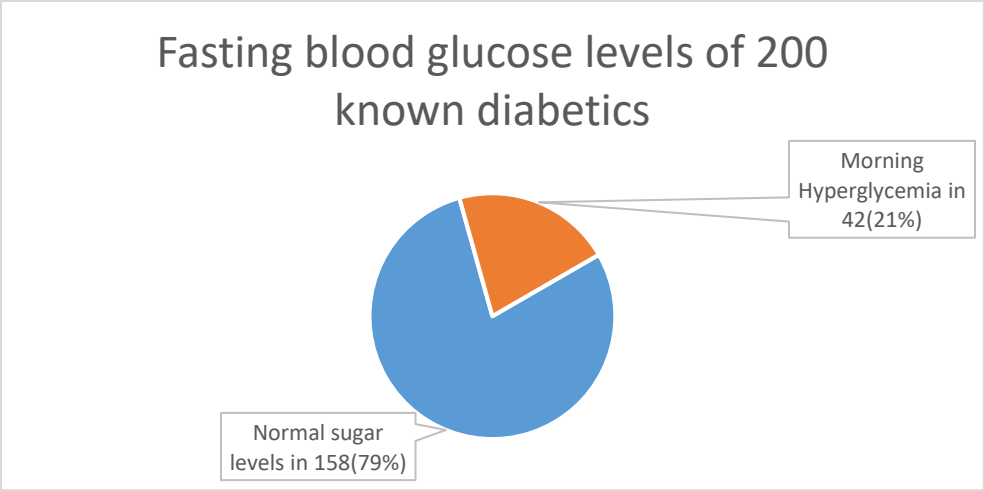
MATERIALS AND METHODS:

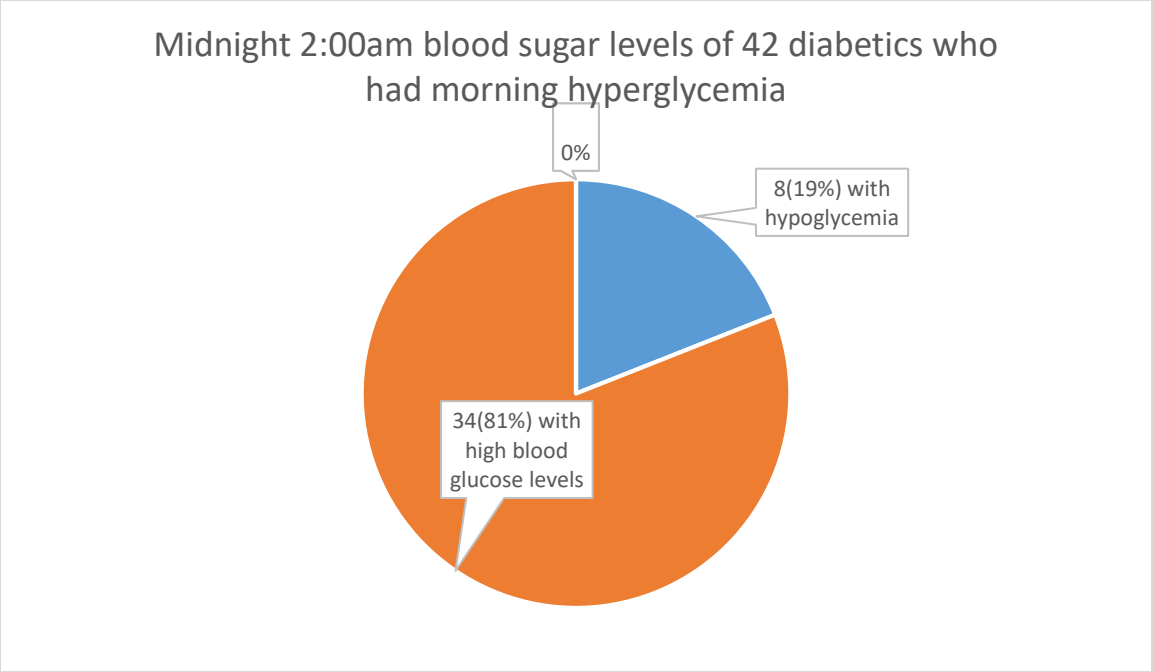
200 known diabetic patients admitted in medical ward were taken as sample by convenient sampling. Fasting blood glucose levels were checked for five consecutive mornings and midnight at 2am with digital glucometer.

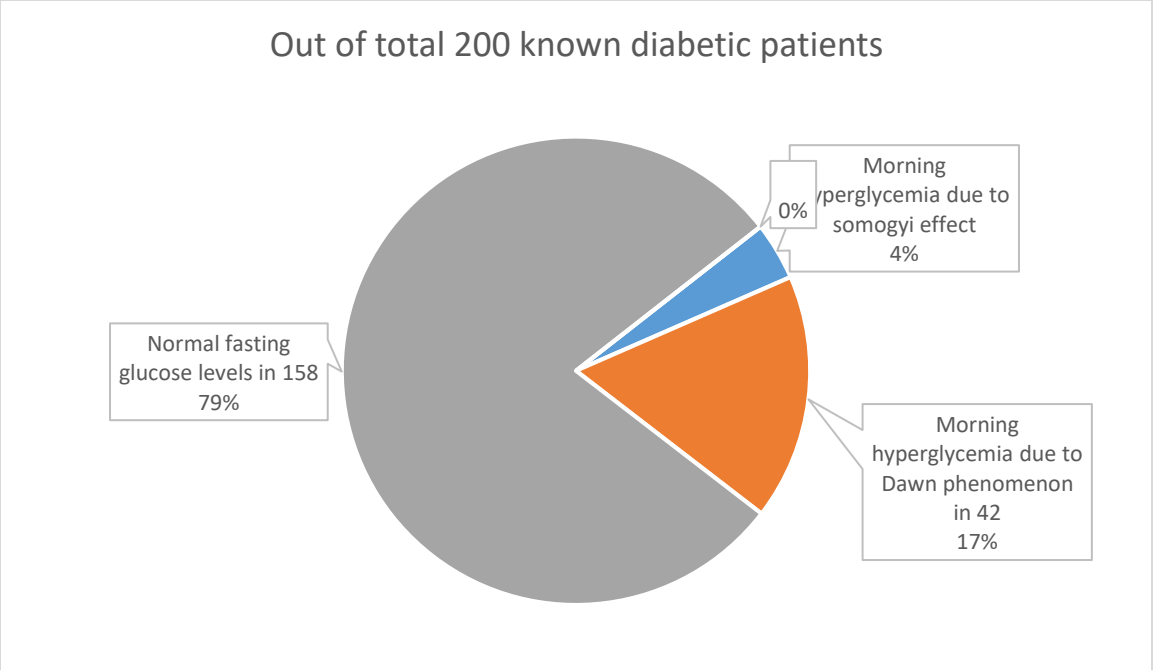
Data Analysis: Data has been analyzed by using SPSS 20.Results will be described in percentage with pie charts.

RESULTS:

Among the sample of 200 patients 42 were found to have morning hyperglycemia and remaining 158 were euglycemic. 34(81%) out of 42 were having high blood glucose levels at 2:00am midnight while 8(19%) were having hypoglycemia at that time. Similar results were found in next mornings and midnights.Out of total 200 patients 34(17%) had morning hyperglycemia due to dawn phenomenon and 8(4% of total) had it because of somogyi effect







CONCLUSION AND RECOMMENDATIONS:

Both the dawn phenomenon and the Somogyi effect are associated with the development of morning hyperglycaemia, but the pathological mechanisms responsible for these effects are different.

Significant number (21%) of selected diabetic patients were experiencing morning hyperglycemia despite of being on insulin therapy. 34(81%) were having it due to Dawn phenomenon. Remaining 8(19%) had it due somogyi effect. The dawn phenomenon is more common than the Somogyi effect. Both types can be easily diagnosed and there

are some methods of treatment and prevention.The best way of preventing these phenomena is good diabetes mellitus control with appropriate insulin therapy. Strict glycemic control is required in diabetics to avoid complications.

Some possible prevention/treatment options for dawn phenomenon are:

1: Increase evening physical activity

2: Increase amount of protein to carbohydrates in the last meal of the day

3: Long-acting insulin analogues like glargine instead of NPH insulin

Similarly, to prevent/treat somogyi effect following measures could be taken:

1: Do not miss dinner

2: More protein than carbohydrates in the last meal of the day

3: Modify(decrease) insulin dosage

4: Long-acting insulin analogues like glargine instead of NPH insulin

5: Go to bed with higher level of plasma glucose than usual

As pathogenesis of these effects is complicated and still to be explored,further research is warranted which may help reduce dawn phenomenon and Somogyi effect.

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