

Addressing Challenges in Insulin Storage: An Ethical Dilemma among Physicians

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Abstract

Background and Aims: Insulin is a temperature-sensitive protein; hence, its potency is highly dependent on appropriate storage. Ideally, insulin should be stored in the refrigerator, but when in use it can be stored at room temperature for up to four weeks. However, room temperatures vary widely across regions and countries, and all rural areas of developing countries like India are not electrified. This study explored physicians' perception of alternative methods for appropriate storage of insulin, such as indigenous storage methods like clay pots. **Methods:** A Study was conducted among 188 Indian physicians attending a diabetes conference in December 2018 to evaluate the feasibility of indigenous storage methods. **Results:** It was observed that although the use of alternate indigenous methods like clay pots was recommended by them, the proportion was low. The awareness of literature on these methods for insulin storage validation was also less than 50%. Owing to the lack of validation studies on indigenous methods, nearly 80% of the physicians felt that they were not confident to recommend them. Besides, the study results highlighted the necessity of conducting an adequate number of validation studies on indigenous methods in the Indian setting, considering their scarcity. **Conclusion:** This is the first time we highlight ethical dilemmas through a study among physicians when they advise non-refrigerator methods for insulin storage, in the event of a lack of electricity supply. It is hoped that results from these studies would highlight ethical dilemmas among physicians and would motivate researchers in this field to conduct studies to validate alternative methods of insulin storage.

Keywords: India, indigenous methods, insulin storage, physicians, study

INTRODUCTION

People from both higher and lower socioeconomic strata of society are affected by the pandemic of diabetes mellitus.^[1] Insulin is typically needed as a medication for those with type 1 diabetes, those with acute illnesses, pregnant women, and others.^[2] Additionally, persons with type 2 diabetes typically need insulin as a therapy option as the disease progresses. Insulin, which is in use, can be kept at room temperature, but insulin which is not in use, should be kept at specific storage conditions to get optimal output.^[3,4] According to the State of Electricity Access Report 2017,^[5] 1.06 billion people still don't have access to electricity. The report also says that at the current pace, the target of universal electrification by 2030 will not be met, especially in Sub-Saharan Africa. Even when electricity is available, not everyone has a refrigerator, which acts as a hindrance to

insulin storage. An important point to note is that refrigerators from non-electric power supply sources are not affordable and are out of the reach of most people. According to Global Access to Cooling in 2020, which involved 54 high-impact countries, at least 3.2 billion people still face cooling access challenges^[6]

Also, in those areas which have access to electricity, they may not have a full or stable connection. According to IDF Life for a Child, in 30 out of 37 low- and lower-middle-income

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countries studied, at least 33% of families with children with diabetes lack access to refrigeration.^[7]

Given the importance of appropriate insulin storage for maintaining adequate glycaemic control, educating persons with diabetes (PwD) on the appropriate temperature and duration of insulin storage is of utmost importance. Therefore, both physicians and PwD, particularly those living in resource-challenged, underserved areas, should be aware of alternate indigenous insulin storage methods.^[8] As physicians have a vital role in prescription and guidance on insulin therapy, a questionnaire-based study was conducted among Indian physicians to assess their awareness of various insulin storage methods and also, evaluate their perceptions on the use of indigenous storage methods as well as their advice to PwD in this regard.

MATERIALS AND METHODS

Study design, period, and setting

A questionnaire-based study was conducted among 188 Indian physicians, who attended a regional diabetes conference during the period, 1st to 4th December 2018. Indian physicians who were practising in the same country were eligible for the study. Physicians willing to participate in the study were included. Using a multiple-choice questionnaire, the study assessed the details of the participating physicians and their awareness of insulin storage methods and practices.

Data collection

1. Data on the details of physicians such as (i) their highest qualification, (ii) whether treating persons with type 2 diabetes, (iii) treating persons with type 1 diabetes and (iv) whether they prescribed insulin to such PwD, were obtained from the study. Apart from physician details, the questionnaire also included details on the advice given by the physicians to the PwD taking insulin regarding insulin storage methods at home and during travel. The questions included (i) the insulin storage method prescribed, (ii) the storage method prescribed while travelling, (iii) regarding awareness of literature about validation of clay-pot storage method, and (iv) whether study plans to validate clay pots and other indigenous methods of insulin storage might be helpful. The result of this study was presented at an international conference and an excerpt of this study was communicated as a correspondence to a reputed journal for wider reach and education (Pande & Thakur, 2022).^[9]

Statistical analysis

Descriptive analysis was used for the questionnaire-based study to determine the percentages of study participants under different categories of response.

The questionnaire details have been depicted in Table 1.

RESULTS

Study participants

All participants completed the study (100%). Out of the 188 eligible physicians contacted for the study, 175 (93.1%)

Table 1: Multiple choice questionnaire used in the survey (n=188)

Questions	Options
Your highest qualification	MBBS MD DM Others (please specify)
Do you treat patients with diabetes?	Yes No
If you treat patients with diabetes, do you prescribe insulin?	Yes No
Do you treat patients with type 1 diabetes?	Yes No
If you prescribe insulin, what method of storage do you prescribe?	Refrigerator Clay pot (matka) Ice bag Thermos flask
What method do you advise while travelling?	Ice pack Thermos flask Ice bag Cool pouch
Are you aware of the literature about the validation of clay pots?	Yes No
Do you think a study plan to see the validation of clay pots and other indigenous methods would help?	Yes No

MBBS=Bachelor of Medicine and Bachelor of Surgery; MD=Doctor of Medicine; DM=Doctor of Medicine; n=total number of responses

Table 2: Proportion of physicians treating diabetes and prescribing insulin (n=188)

Physicians	Number	Percentage of total
Total eligible	188	100%
Treating diabetes	175	93.1%
Insulin prescribers	163/175 (93.14%)	
Insulin non-prescribers	12/175 (6.86%)	
Not treating diabetes	13	7%

n=total number of responses

were treating PwD, while 13 (7%) were not [Table 2]. Among the 175 physicians who treated PwD, 163 (93.14%) were insulin prescribers, and 12 (6.86%) physicians did not prescribe insulin therapy to their PwD [Table 2].

Prescribed methods of insulin storage at home

The majority of the physicians contacted for the study, that is, 111 out of 188 (59%) physicians prescribed the use of a refrigerator to the PwD for storage of insulin at home. When refrigerator facilities were unavailable 55 (29%) physicians prescribed mixed methods for insulin storage at home, 8 (5%) physicians prescribed ice bags, 6 (3%) physicians prescribed clay pots, 2 (1%) prescribed thermos flasks, and the remaining 6 (3%) physicians had no answer [Figure 1].

Prescribed methods of insulin storage while travelling

The number of physicians prescribing the use of ice packs and clay pots for storing insulin while travelling was found to be

the same, that is, 45 out of 188 (24%) physicians in both cases. The use of a thermos flask while travelling was prescribed by 36 (19%) physicians and ice bags by 20 (11%) physicians. The remaining physicians had either no clear preference or no answer regarding the storage of insulin while travelling [Figure 2].

Awareness among physicians regarding literature on validation of insulin storage

In response to the question regarding the validation of the clay pot method and other indigenous methods of insulin storage, 87 (46%) physicians mentioned that they were aware of such validation methods, while 94 (50%) physicians were not. The remaining 7 physicians (4%) had no answer to this question [Figure 3].

Physicians' views regarding the need for validation studies for indigenous storage methods

Among all the physicians, 147 (78%) physicians wanted further validation data to gain confidence for prescribing indigenous insulin storage methods, while 29 (16%) physicians opined that no such validation data was needed [Figure 4].

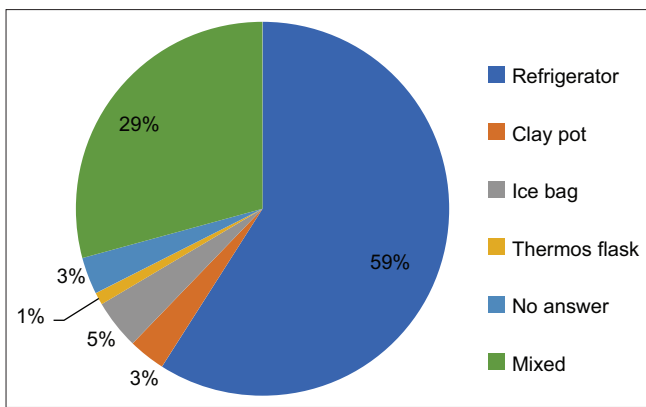


Figure 1: Prescribed methods of insulin storage at home. *n*: total number of responses. Note: The exact percentages for each method prescribed are as follows: refrigerator (59%), clay pot (3.2%), ice bag (4.3%), thermos flask (1.1%), no answer (3.2%) and mixed (29.3%)

DISCUSSION

Given the crucial role of appropriate storage methods for achieving the desired effects of insulin therapy and the pivotal role of physicians in the context of prescribing insulin storage methods, the present study was performed to study prescription patterns and perceptions of 188 Indian physicians for insulin storage. Among the physicians enrolled in the study, around 93% treated PwD, among which 93.14% were insulin prescribers. These findings indicate that the prescription of insulin therapy is common among Indian physicians who treat PwD.

Regarding the prescription of storage methods for insulin, the majority of the physicians (59%) prescribed the use of a refrigerator at home, and the use of ice packs (24%) and clay pots (24%) was most commonly prescribed while travelling. Since electricity supply is still a constraint in certain regions of the world,^[10] the use of indigenous methods like clay pots is a better alternative option for insulin storage. It is advised

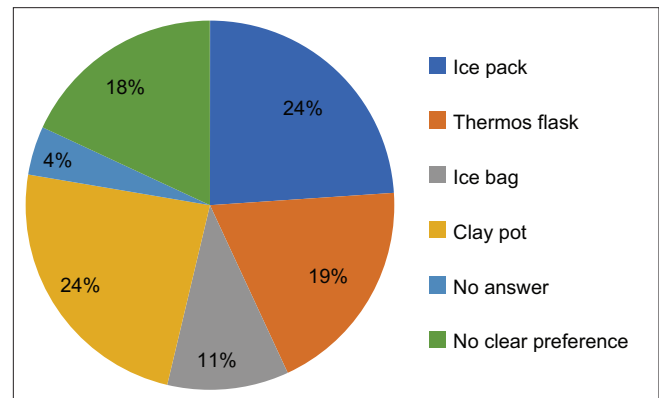


Figure 2: Prescribed methods of insulin storage while travelling. *n*: total number of responses. Note: The exact percentages for each method prescribed are as follows: ice pack (29.9%), thermos flask (19.2%), ice bag (10.6%), clay pot (23.9%), no answer (4.3%) and no clear preference (18.1%)

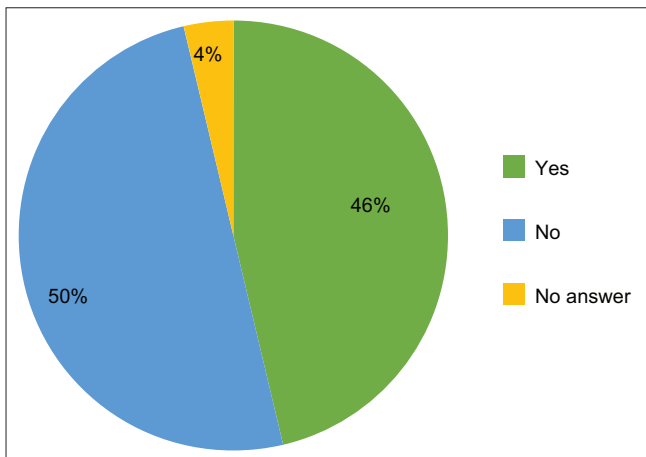


Figure 3: Awareness regarding literature on insulin storage validation. *n*: total number of responses

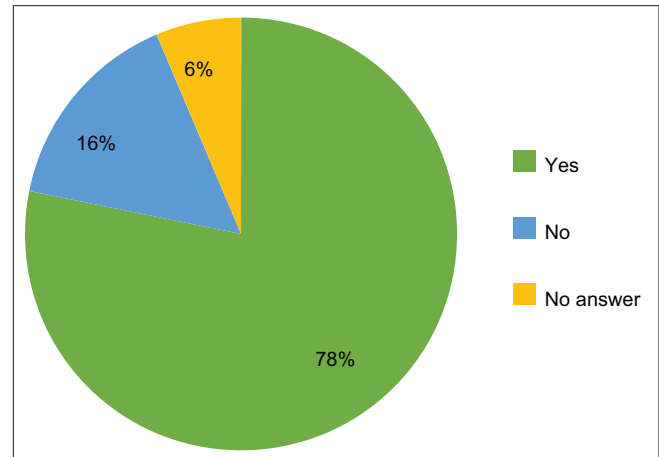


Figure 4: Opinion on the need for validation studies. *n*: total number of responses

that in the absence of refrigerators, insulin should be kept in a dark place with no humidity, moisture, and minimum or no exposure to direct heat sources or sun rays.^[11] Based on this, several traditional and unconventional methods of insulin storage have been developed and are used in different countries, such as India, Tanzania, Sudan, Pakistan, Mali, Ethiopia, and Haiti.^[3] Clay pots filled with water for evaporative cooling to store insulin are most commonly used by thousands of families in resource-limited countries.^[11] The different variants of unconventional methods of insulin storage include pot-in-pot refrigerators or the Zeer pot, mud pots, goat skin pots filled with water,^[11] vegetable gourds filled with water, and buckets filled with wet sand.^[3] It has been observed that the temperatures achieved by these devices are at or near room temperature, even in hot climates. However, evaporative cooling allows for humidity, and these devices are more efficacious at lower humidity.^[3] In this study, one-fourth of the physicians prescribing insulin advised the use of clay pots for insulin storage in the absence of electricity.

As per the United States Pharmacopeia (USP)/the United States Food and Drug Administration (FDA) criteria, a minimum of 95% intact insulin (equivalent to 95 U/mL) is required upon release.^[12] Therefore, quantitatively, the amount of intact insulin is measured in multiple ways.^[12,13] It is important to note that most studies on insulin stability have been conducted in western countries where room temperature is usually below 25°C. On the other hand, in tropical countries, room temperatures are normally higher.^[14] In India, the temperature remains well above 25°C in some parts, for most of the year. Under these circumstances, the extrapolation of data from studies of western countries to the Indian environment is questionable.^[15] Unfortunately, very few studies have assessed the effects of higher room temperatures on insulin quality.^[14] The cut-off value for the acceptable decrease in insulin potency, as recommended by the Indian Pharmacopoeia, is 10%. However, a study by Vimalavathini *et al.*^[15] demonstrated that at higher temperatures (32°C and 37°C), the potency of both regular and biphasic insulin from different brands decreased by 14%–18% after three weeks. This study revealed that in the absence of a refrigerator, insulin can be stored at room temperature for up to two weeks under Indian conditions.

In India, individuals from rural areas who do not have refrigerator facilities are advised by health professionals to store insulin in mud pots. The inside temperature of mud pots is typically a few degrees lower than the ambient room temperature. However, during summers, with the increase in room temperature, the inside temperature can rise even beyond 35°C. Under such conditions, insulin stored in a mud pot is not protected from denaturation.^[16] Therefore, it is essential to develop more indigenous methods for proper insulin storage suitable for the diverse climatic conditions across the country. Moreover, validation of indigenous methods using different methods such as bioassay on type 1 diabetic cell lines and mouse models should also be emphasised, to promote the prescription of indigenous methods in the country.^[17]

Nearly 80% of the physicians in our study wanted validation studies for understanding insulin stability while using indigenous methods of storage like clay pots. This finding asserts the utmost need for validation of indigenous methods for insulin storage, to promote their prescription by physicians among individuals on insulin therapy both at home and while travelling. The key summary points and recommendations developed from the study have been highlighted in Table 3. This study highlights this ethical dilemma, which is seen in nearly 80% of physicians who advise non-refrigerator methods for insulin storage in the event of a lack of electricity supply or availability of a refrigerator.

Strengths and limitations of the study

To the best of our knowledge, this is the first study on the perception of insulin storage methods among physicians. This serves as the main strength of the present study. In addition, a large number of insulin-prescribing physicians (175) contacted for the study exclusively from a developing country, that is, India also added novelty to the study. Since in developing countries, the availability of electricity and the inability to purchase refrigerators are major limiting factors for the storage of insulin, the emphasis on the evaluation of indigenous storage methods prescribed by the physicians in the study also adds value to the study.

However, this study has a few limitations. Being a questionnaire-based study, the possibility that a few physicians might have answered casually could not be ruled out. To overcome this limitation, a larger number of physicians were included in the study. The analysis also included physicians who did not treat diabetes or who were non-insulin prescribers. These physicians participated and completed the study based on their knowledge and perceptions, rather than actual clinical practice. Also, demographic data of the physicians were not included in the study, such as years of clinical experience, age, and gender. Hence, the impact of these factors in addition to their highest qualification on insulin storage prescribing practises, and awareness of indigenous storage methods and validation studies could not be assessed. In addition, the analysis of prescribing methods and awareness of insulin storage methods among physicians practising in rural vs urban locations was also beyond the scope of this study as many physicians see PwD from both rural and urban areas so this demarcation is easily possible. Studies in this regard would

Table 3: Key summary points and recommendations from the survey

The first survey on the perception of insulin storage among physicians from India
In the absence of electricity and refrigerators, clay pots were prescribed for insulin storage by one-fourth of the physicians.
More than three-fourths of the physicians wanted a validation study for understanding insulin stability with indigenous methods.
Need for validation studies on various indigenous storage techniques
Further studies are required on insulin analogues for overcoming the temperature-sensitivity issue of insulin.

provide additional insights into indigenous insulin storage practises in rural regions of India since physicians practising in those regions are more likely to understand the specific needs of insulin users living in rural and remote regions of the country.

CONCLUSIONS AND FUTURE PERSPECTIVE

For PwD, proper insulin storage is a critical determinant for ensuring blood glucose control. The use of a refrigerator is the ideal method of insulin storage. However, alternate methods are required in developing countries where access to electricity is not complete. The study among physicians revealed that although indigenous methods are prescribed for insulin storage, awareness of insulin validation is low. Again nearly 80% of physicians lacked confidence in prescribing indigenous methods of insulin storage, owing to a lack of adequate validation studies on those methods. Most of the studies on insulin storage validation have been performed in western countries, and hence, such data cannot be extrapolated to Indian conditions.

It is hoped that results from these studies will highlight the physician's ethical dilemma and will motivate researchers in this field to conduct studies to validate alternative methods of insulin storage. Until further studies are done, we believe that there are a few studies already done in this field; physicians should be educated and made aware of such studies. So, when refrigeration is not an option and it becomes necessary to advise the non-refrigerator method of insulin storage, they can advocate it with more conviction.

The theme for World Diabetes Day 2021–23 is access to diabetes care, which is still a very pertinent one a century after the discovery of insulin. To increase access to insulin for all PwD, regardless of where they live, we believe that physicians who prescribe insulin need to have a better awareness of and trust in the various insulin storage methods.

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