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Regular Physical Activity Improves Ability to Tolerate Pain

Individuals who lead a physically active lifestyle have better pain tolerance than their counterparts who were sedentary, suggests a study from Norway, which surveyed over 10,000 participants published May 24, 2023 in the journal *PLoS One*.¹ Those who engaged in higher levels of activity had a higher level of pain tolerance.

Arnes et al examined data of 10,732 residents from Norway from the 6th (2007-2008) and the 7th (2015-2016) rounds of the Tromsø Study. Fifty-one percent of them were women. The participants self-reported their physical activity levels (sedentary, light, moderate or vigorous) through questionnaires including their levels of pain tolerance, which was assessed by the cold-pressor test, where the participants were asked to dip their hands in cold water. Their objective was to determine if the level of physical activity and change in physical activity had any impact on pain tolerance.

Results showed that the study subjects who were physically active could tolerate pain better than those who reported a sedentary lifestyle in both rounds of the Tromsø Study. Light (6.7 s), moderate (14.1 s) and vigorous (16.3 s) physical groups had higher pain

tolerance than the sedentary group indicating that the pain tolerance was significantly higher among those reporting higher total activity levels. Those who were more active between 2015 and 2016 had higher overall levels of pain tolerance. But the association of change in level of physical activity and pain tolerance was not statistically significant in both rounds of the survey.

These findings have added yet another benefit of physical activity to the already well-established list of beneficial effects. Any change in the level of physical activity from lower to higher may be associated with higher pain tolerance than vice versa. Increasing physical activity may therefore help alleviate chronic pain by increasing pain tolerance. Whether this is a cause-and-effect association needs to be verified in further studies. Nonetheless, regular physical activity is beneficial for overall improvement in health and well-being, both physical and mental.

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The Pyinsa Rupa Model of Diabetes Care: Inspiration from Myanmar

ABSTRACT

In this communication, we describe the Pyinsa Rupa, the famous mythical hybrid animal of Myanmar culture and history. This animal integrates various features of the lion, elephant, deer, ngagyin fish and hintha bird, into one composite creature. We utilize the unique characteristics of these animals: strength, sustainability, sociability, safety and swiftness, to craft a model that can serve as a beacon for diabetes care and diabetes care delivery.

Keywords: Diabetes, diabetes care delivery, glycemic pentad, Myanmar, person-centered care, psychosocial issues, South East Asia

Myanmar is a country rich in history and tradition. Traditional Myanmar wisdom, with its quintessential relevance, can help in tackling many of the challenges that we face in the modern world. One such health-related issue is diabetes. In this opinion piece, we utilize the Pyinsa Rupa, the famous mythical hybrid animal of Myanmar,¹ to create a culturally relevant model for holistic diabetes care delivery, for appropriate choice of targets and techniques in diabetes management, and for rational evaluation of various glucose-lowering interventions.

THE PYINSA RUPA

The Pyinsa Rupa is a mythical hybrid of five animals.¹ These include three terrestrial animals – the lion, elephant and water buffalo, one aquatic creature – the ngagyin fish (white carp) and one flying bird – the hintha bird. Thus, the five components of Pyinsa Rupa

are a comprehensive mix of the various classes of the animal kingdom.

These five animals are known for various characteristics: the lion for its strength, the elephant for its sustainability and the water buffalo for its sociability. The ngagyin fish, which swims in the depths of the ocean, represents safety, while the hintha bird, which flies in the skies, stands for swiftness and speed. We use the Pyinsa Rupa to create a glycemic compass, which helps create a roadmap for us, a glycemic mirror of sorts, that allows us to analyze and audit our activities in an objective manner and a glycemic beacon, that lights the way ahead.

THE HEALTH CARE ECOSYSTEM

The Pyinsa Rupa reminds us that the health care ecosystem, and specifically the diabetes care ecosystem that we create, should be strong or robust, sustainable or durable, and ‘sociable’ or concordant with other

aspects of health care. For example, integrating diabetes care into ongoing noncommunicable disease (NCD) prevention programs may be more effective and efficient than creating a separate vertical for diabetes care at the primary level.² An ideal diabetes care system should also offer swift and speedy results, while ensuring safety and security of the population being addressed.

DIABETES CARE STRATEGIES

Diabetes care strategies have to be individualized for each person living with the syndrome. The targets of therapy, and techniques used for treatment have to be tailored to meet the person's unique needs. The Pyinsa Rupa assists in this endeavor, by reminding us of the need to balance strength and swiftness with safety and sustainability.³ In most adults, a target glycated hemoglobin (HbA1c) of <7% is advisable. Examples include elderly persons, those with established vascular complications, and individuals with hypoglycemia unawareness. At the same time, some persons, e.g., women in pre-conception and antenatal phase of life will benefit from stricter targets.

CHOICE OF GLUCOSE-LOWERING REGIMENS

The Pyinsa Rupa teaches us to craft combinations that are able to address the glycemic pentad: control of fasting glucose, postprandial glucose and HbA1c, along with safety-minimizing glycemic variability and avoiding hypoglycemia.⁴ An example of a five-pronged management strategy is dietary advice, exercise, an insulin sensitizer, a sulfonylurea or dipeptidyl peptidase 4 inhibitors and a basal insulin.

It also reminds the treating physician to choose combinations of glucose-lowering drugs with care, based upon

their mechanism of action. For example, a combination of two sulfonylureas, or premixed insulin and glargine may not be an appropriate choice. On the other hand, crafting a "smart" combination of glargine with oral glucose-lowering drugs and/or rapid-acting insulin lives up to the 'standards' of the Pyinsa Rupa.⁵

SUMMARY

The Pyinsa Rupa, an integral part of Myanmar culture, continues to inspire countless artists and thinkers. We utilize the five animals of Pyinsa Rupa, with their unique characteristics and strengths, combined in the spirit of teamwork and concordance, to create a culturally relevant model for diabetes care delivery. We hope that this model will contribute to the betterment of diabetes control, not only in Myanmar, but beyond as well.

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STAR (Survey for ManagementT of DiAbetes with FibeR-rich Nutrition Drink): A Pan India Survey to Understand the Physician and Patient Perspective Regarding the Role of Dietary Fiber Supplement in the Management of Type 2 Diabetes

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ABSTRACT

Objectives: The aim of the STAR survey was to understand the physicians' knowledge, attitude and perception regarding the role of nutritional dietary fiber supplements in the daily management of type 2 diabetes mellitus (T2DM). It also aimed to compare the changes in glycemic parameters as well as energy and satiety levels between patients taking a high-fiber supplement and those not taking a fiber supplement. **Methods:** Two cross-sectional pan-India surveys were conducted. The first was among 152 physicians who had >5 years of experience in treating patients with T2DM and treated >50 patients with T2DM per month. A self-administered paper-based questionnaire was used for the survey. The other survey was conducted among 3,042 patients with T2DM who were receiving treatment with antidiabetics. These patients were further categorized into the Horlicks Diabetes Plus (HDP) group, which consisted of 1,524 patients who had consumed the HDP fiber supplement for a minimum of 3 months and the non-HDP group, which included 1,518 patients who had never consumed HDP. **Results:** Almost all physicians prescribed fiber-rich nutritional supplements to their patients with T2DM and believed that dietary fiber has an important role in managing glycated hemoglobin (HbA1c) values, healthy weight and cholesterol levels. Among the main benefits of HDP seen by physicians were improvement in satiety levels and increase in physical activity, reduction in HbA1c, fasting and postprandial glucose, and reduction in dose and/or number of hypoglycemic medications. All physicians recommended that it was important to increase awareness among patients as well as doctors regarding the benefits of HDP in patients with T2DM. Patients in the HDP group reported a mean decrease of 0.72 in their HbA1c value which was statistically significant at 3 months (8.04 at baseline to 7.32 at 3 months). In contrast, the non-HDP group showed a non-statistically significant decrease of 0.61 in HbA1c from a baseline value of 8.15. Furthermore, patients reported a significant decrease in weight of 3 kg in 3 months from baseline value of 72.11 kg to 69.11 kg. This reduction in weight was observed in 82% patients in the HDP group, while the non-HDP group showed an insignificant weight reduction from a baseline value of 72.14 kg to 71.46 kg in 3 months. About 83% of patients reported feeling full for longer periods of time and 92.62% reported feeling more energetic after starting HDP. The compliance and satisfaction rates with HDP were 96% and 75%, respectively. **Conclusion:** A high-fiber supplement taken along with patients' existing antidiabetic treatment plan has the potential to decrease glycemic parameters and weight while increase the satiety and energy levels among patients with T2DM. However, these results need to be evaluated further with long-term clinical studies conducted in the real world.

Keywords: Dietary fiber, type 2 diabetes, high-fiber supplement, glycemic outcomes, satiety, physical energy

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In 2021, globally, an estimated 537 million adults aged 20 to 79 years had diabetes, most of which was type 2 diabetes (T2DM).¹ According to the 2021 International Diabetes Federation (IDF) report, India had the second largest number of adults with diabetes in the world (74.2 million). Further, it was estimated that by 2045, there will be approximately 124.9 million patients with diabetes aged 20 to 79 years in India.² The "Asian Indian Phenotype" has higher rates of central obesity and

increased visceral fat, which are the main causes of insulin resistance (IR).³ Among Indian patients with diabetes, about 69% fail to achieve the target level of glycated hemoglobin (HbA1c).⁴ Lifestyle modification is central to the prevention and management of T2DM.⁵ The American Diabetes Association (ADA), Research Society for the Study of Diabetes in India (RSSDI) and Indian Council of Medical Research (ICMR) clinical practice guidelines emphasize diet modification as a first-line therapy for treating T2DM and provide recommendations for daily nutritional needs. Weight loss⁶⁻⁸ reduces blood glucose besides improving major risk factors of cardiac disease like blood pressure and lipids (cholesterol, triglycerides and low-density lipoproteins [LDL]).^{9,10} Weight loss is also important because within 6 years from diagnosis, >80% of patients with T2DM can achieve remission by losing >15 kg of body weight;^{11,12} however, this likelihood is lower with increased time since diagnosis.⁵ Dietary fiber reduces the risk of obesity and in turn T2DM,¹³ because excessive calorie intake leading to obesity is one of the strongest predictors for T2DM.^{14,15} Therefore, any nutritional intervention that results in modest weight loss reduces IR.¹⁶ Unhealthy diets are often lacking in fiber-rich foods.¹⁷ The ADA recommends that fiber intake in patients with diabetes should be about 14 g fiber/1,000 kcal daily, or about 25 g/day for women and 38 g/day for men.¹⁸ The Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD) has also recommended that dietary fiber intake should be at least 35 g/day (4 g/1,000 KJ). The group also recommends fiber-enriched foods and supplements when adequate intake cannot be obtained from diet alone.⁵ RSSDI recommends a fiber intake of 25 to 40 g/day for Indians.⁷

Dietary fiber can be classified as soluble or insoluble according to its solubility in water. Soluble dietary fiber forms a gel-like substance in the gastrointestinal (GI) tract thereby increasing the viscosity of GI contents. This prolongs the transit time, digestion and absorption of GI contents.¹³ Moreover, high-fiber diets have lower calories for the same portion size.¹³ Moreover, foods high in fiber need more chewing before swallowing. This slows down the rate of food consumption and leads to feelings of satiety due to the release of gut hormones.^{19,20} Soluble dietary fiber has been specifically linked to increased feelings of satiety and a reduced overall energy intake;²¹ it also increases the duration for which satiety signals are released.²² The viscous gel formed by the fiber acts as a diffusion barrier,²³ reducing the rate at which glucose is absorbed into the

bloodstream, and thus decreases postprandial blood glucose levels.²⁴

Despite dietary recommendations, people consume inadequate amounts or incorrect type of dietary fiber.³ A study that compared the Indian diet with EAT-Lancet reference diet, reported that Indian diets were unhealthy across all states and income categories. Moreover, the fiber intake was found to be much lower than the recommended level in women (15-30 g/d) across all income groups.²⁵

We conducted the STAR survey among physicians treating patients with diabetes as well as among patients with diabetes. The objective of the physicians' survey was to obtain an understanding of their knowledge, attitude and perception regarding the role of nutritional dietary fiber supplements in the daily management of T2DM. The objectives of the patients' survey were to compare the changes in glycemic parameters as well as energy and satiety levels between patients taking a high-fiber supplement and those not taking a fiber supplement.

METHODS

Design and Participants

To achieve the study objectives, two cross-sectional pan-India surveys were conducted between March 2023 and May 2023. A convenient sample of 152 physicians who had ≥ 5 years of experience in treating patients with T2DM, treated ≥ 50 patients with T2DM per month, and provided their written consent to participate were enrolled in the survey. A self-administered paper-based questionnaire was shared with them for completion. The quantitative survey consisted of 26 questions (median time to completion 10 minutes) which included multiple choice, short answers using free text, yes/no and 7-point Likert response scales. The survey questions were designed to understand their knowledge, attitude and perception regarding the role of nutritional dietary fiber supplements in the daily management of T2DM. More specifically, the survey included questions to understand the segment of patients with T2DM who would benefit the most from consumption of dietary fiber supplement such as Horlicks Diabetes Plus (HDP), the recommended dose/quantity of HDP along with the preferred medium of consumption and the observed benefits of consuming HDP with respect to parameters such as reduction in HbA1c, improvement in physical energy and improvement in satiety levels in patients with T2DM.

The other survey was conducted among 3,042 patients with T2DM in the outpatient clinics of participating doctors. Each participating doctor recommended a total of 20 patients from his/her practice for the survey. Of the 20 patients that (s) he recommended, 10 patients were consuming HDP as their primary source of dietary fiber supplement for a minimum of 3 months while the remaining 10 were not consuming HDP. However, all patients were receiving pharmacological treatment for diabetes. The criteria were, age ≥ 18 years, diagnosis of T2DM ≥ 12 months before participation, ongoing treatment for T2DM with oral antidiabetics and/or insulin and provision of written informed consent. These patients were further categorized into the HDP group, in which the patients had consumed the HDP supplements for a minimum of 3 months and the non-HDP group in which the patients had never consumed HDP. Based on whether the patient consumed HDP or not, they were provided different self-administered paper-based questionnaires each consisting of about 40 questions (median time to completion 30 minutes) and included multiple choice, short answers using free text, yes/no and 5-point Likert response scales. Both patient surveys included questions regarding sociodemographic and clinical characteristics, diet and lifestyle, their knowledge regarding the role of dietary fiber in the management of T2DM, their consumption of fiber or fiber supplements – type and quantity, their energy levels while performing day-to-day physical activities, and their satiety levels. In addition to the above questions, patients were requested to provide their current HbA1c, fasting glucose, postprandial glucose values and recall values for these parameters prior to consuming HDP to the best of their ability. Patients in the HDP group were also asked to rate their current physical energy and satiety levels after starting HDP. Lastly, for patients in the HDP group, the survey also asked questions with respect to compliance and level of satisfaction with HDP. All responses were kept anonymous, and the identity of the sponsor of the survey was not revealed to the respondents. Participation in the survey was voluntary and respondents had an option to exit the survey at any point. Institutional Review Board approval was not required because this was considered a market research study.

Statistical Analyses

Data was analyzed using descriptive analyses such as frequencies for categorical variables and mean (standard deviation [SD]) for continuous variables to summarize responses from the physician and patient surveys. For surveys obtained from patients, a within and between

group comparisons were conducted. For the HDP group, a within group comparison using the paired *t*-test to estimate the mean change in weight, HbA1c, fasting glucose and postprandial glucose values from before starting HDP (baseline values) to after starting HDP. Furthermore, a between group comparison (HDP group vs. non-HDP group) was conducted using an independent *t*-test to compare the mean difference in weight, HbA1c, fasting glucose and postprandial glucose values between the two groups. A type 1 error level of 5% ($p < 0.05$) was established for inferential analyses. Statistical Package for Social Sciences (SPSS) for Windows version 10.0 (SPSS Inc., Chicago) was used for the analyses.

RESULTS

Physician Survey

Of the 152 doctors who participated in the survey, 41% were diabetologists, 54% were general practitioners and 5% were endocrinologists. The mean duration of experience was 20 years. Almost all the physicians prescribed fiber-rich nutritional supplements to their patients with T2DM, and believed that dietary fiber has an important role in managing HbA1c values, healthy weight and cholesterol levels. Though most physicians (77%) recommend consuming 30-45 g of fiber/day, most of their patients (about 71%) consume <15 g of fiber daily. This is mainly due to the lack of awareness about the benefits of fiber in managing T2DM. Most patients lack knowledge regarding food items and nutritional supplements rich in fiber. Hence, awareness regarding the role of fiber and fiber-rich supplements in managing diabetes among patients needs to be increased.

Opinion about role of HDP in management of diabetes: Recommended dose and observed benefits

Physicians reported that they recommend HDP to about 50% of patients with T2DM, 35% of patients with overweight and 40% of patients with obesity. They recommend consuming 15-30 g of HDP to patients with T2DM with HbA1c $<8\%$ and 15-45 g to patients with HbA1c $>8\%$. For patients with overweight and obesity, they recommend 30-45 g of HDP on a regular basis. Based on the patients' body mass index (BMI) and preference, about 57% of physicians recommend consuming HDP with milk, while 43% recommend consuming it with water. When asked about the top three benefits of HDP in their experience, about 98% of physicians reported improvement in satiety levels and increase in physical activity to be the topmost benefit, followed by reduction in HbA1c, fasting

glucose and postprandial glucose (91%) and reduction in dose and/or number of hypoglycemic medications (75%) after consuming HDP for 3 to 6 months. Lastly, physicians reported that most of their patients (96%) were compliant and consumed HDP on a regular basis. Among those who did not consume HDP regularly or discontinued, added financial burden was one of the main reasons followed by no change in their clinical parameters or energy levels after initiating HDP. All participating physicians recommended that it was important to increase awareness among patients as well as doctors regarding the benefits of HDP in patients with T2DM through social media, educational campaigns, counseling programs and other channels.

Patient Survey

There were 1,524 patients in the non-HDP group and 1,518 patients in the HDP group. The mean age of patients was 55.64 years and 56.3 years, respectively, and almost 57% were male. More than 70% of the patients were overweight or obesity. The baseline demographic and clinical characteristics are shown in Table 1.

Glycemic outcomes at 3 months

A statistically significant reduction of 0.72 in HbA1c was observed at 3 months from baseline in the HDP group. The decrease in HbA1c at 3 months was 0.61 in the non-HDP group; however, this was not statistically significant. A significant decrease in weight of 3 kg in 3 months from baseline was observed in 82% patients in the HDP group, while no significant weight reduction was reported in the non-HDP group (Table 2).

Change in satiety and physical energy levels

A total of 83% patients in the HDP group reported feeling full for longer periods of time after starting HDP vs. only 42% patients in the non-HDP group feeling full. There was a 25% and 23% increase in number of patients who reported feeling satisfied and full after a meal, respectively from baseline to 3 months in the HDP group (Table 3). Similarly, about 93% patients in the HDP group reported improvement in energy levels after starting HDP and 67% patients reported moderate to high increase in energy levels post consumption of HDP at 3 months. In contrast, 85% patients reported feeling fatigued and tired in the non-HDP group (Table 3).

Awareness about benefits of consuming a high-fiber diet

Overall, 85% of patients in the HDP group were aware about the benefits of consuming a high-fiber diet for

Table 1. Baseline Characteristics of Patients

Parameters	Non-HDP group	HDP group
Total (N)	1,524	1,518
Mean age (years)	55.64	56.30
Male, n (%)	861 (56.49)	855 (56.32)
Female, n (%)	661 (43.37)	657 (43.28)
Family history of diabetes, n (%)	1,022 (67)	1,039 (68.44)
HDL, n (%)		
<30	495 (32.48)	531 (34.98)
30-59	879 (57.67)	854 (56.25)
≥60	137 (8.98)	112 (7.37)
Duration of T2DM, n (%)		
≤5 years	618 (40.55)	565 (37.22)
6-10 years	487 (31.95)	545 (35.90)
11-15 years	235 (15.41)	234 (15.41)
16-20 years	101 (6.62)	86 (5.66)
>20 years	79 (5.18)	79 (5.20)
Blood pressure, mmHg, (mean)		
Systolic	137	135
Diastolic	87	85
HbA1c, mean (SD)	8.15 (1.79)	8.04 (1.32)
Weight, mean (SD)	72.14 (13.08)	72.11 (12.25)
BMI (kg/m²), n (%)		
Mean	27.43	27.32
Normal weight (18.5-24.9)	438 (28.74)	426 (28.06)
Overweight (25-29.9)	685 (44.94)	758 (49.93)
Obesity (≥30)	355 (23.29)	309 (20.35)
PPG (mg/dL), n (%)		
Mean	204	206
Normal (≤140)	211 (13.84)	199 (13.10)
Prediabetic (≥141-≤200)	686 (45.01)	650 (42.81)
People with diabetes (≥201)	621 (40.74)	657 (43.28)
FPG (mg/dL), n (%)		
<125	280 (18.37)	216 (14.22)
125-199	881 (57.80)	921 (60.67)
200-299	299 (19.61)	332 (21.87)
≥300	46 (3.01)	46 (3.03)

HDL = High-density lipoprotein; T2DM = Type 2 diabetes mellitus; HbA1c = Glycated hemoglobin; SD = Standard deviation; BMI = Body mass index; PPG = Postprandial glucose; FPG = Fasting plasma glucose.

managing diabetes vs. 67.45% in the non-HDP group. In the non-HDP group, 91.14% of patients were inclined to take high-fiber supplements when prescribed by a doctor after explaining their health benefits.

Table 2. Outcomes at 3 Months

Parameters	Non-HDP group		HDP group			
	Baseline	At 3 months	Baseline	At 3 months		
BMI (kg/m²), n (%)						
Mean	27.43	27.19	27.32	26.20		
Normal weight (18.5-24.9)	438 (28.74)	472 (30.97)	426 (28.06)	570 (37.54)		
Overweight (25-29.9)	685 (44.94)	663 (43.50)	758 (49.93)	659 (43.41)		
Obesity (≥30)	355 (23.29)	327 (21.45)	309 (20.35)	228 (15.01)		
PPG (mg/dL), n (%)						
Mean	204	181	206	153		
Normal (≤140)	211 (13.84)	423 (27.75)	199 (13.10)	528 (34.78)		
Prediabetic (≥141-≤200)	686 (45.01)	666 (43.70)	650 (42.81)	681 (44.86)		
Diabetic (≥201)	621 (40.74)	428 (28.08)	657 (43.28)	300 (19.76)		
FPG (mg/dL), n (%)						
<125	280 (18.37)	473 (31.03)	216 (14.22)	631 (41.56)		
125-199	881 (57.80)	731 (47.96)	921 (60.67)	732 (48.22)		
200-299	299 (19.61)	172 (11.28)	332 (21.87)	133 (8.76)		
≥300	46 (3.01)	31 (2.03)	46 (3.03)	12 (0.79)		
		P value		P value		
HbA1c, mean (SD)	8.15 (1.79)	7.54 (1.50)	0.031	8.04 (1.32)	7.32 (1.08)	<0.001
Weight, mean (SD)	72.14 (13.08)	71.46 (12.30)	0.056	72.11 (12.25)	69.11 (11.71)	<0.001

Table 3. Changes in Satiety and Physical Energy Levels at 3 Months Reported by HDP Patients

	Baseline	At 3 months	Change from baseline
Satiety levels, n (%)			
Starving, no energy, very weak	17 (1.12)	2 (0.13)	-0.99
Very hungry	45 (2.96)	11 (0.73)	-2.23
Uncomfortably hungry	149 (9.82)	16 (1.06)	-8.76
Hungry, stomach growing	364 (24.0)	23 (1.53)	-22.47
Starting to feel hungry	368 (24.2)	84 (5.57)	-18.63
Satisfied	401 (26.4)	782 (51.89)	25.49
Full	117 (7.71)	467 (30.99)	23.28
Overfull	30 (1.98)	91 (6.04)	4.06
Stuffed	13 (0.86)	22 (1.46)	0.60
Extremely stuffed	3 (0.20)	9 (0.6)	0.40
Missing	11 (0.72)	11 (0.72)	-
Physical energy levels, n (%)			
Not at all energetic	101 (6.65)	7 (0.46)	-6.19
Somewhat energetic	453 (29.8)	98 (6.46)	-23.34
Neutral	589 (38.8)	257 (16.93)	-21.87
Moderate energy	341 (22.5)	901 (64.08)	37.51
High energy	20 (1.32)	105 (6.92)	5.60
Missing	14 (0.92)	140 (9.22)	-

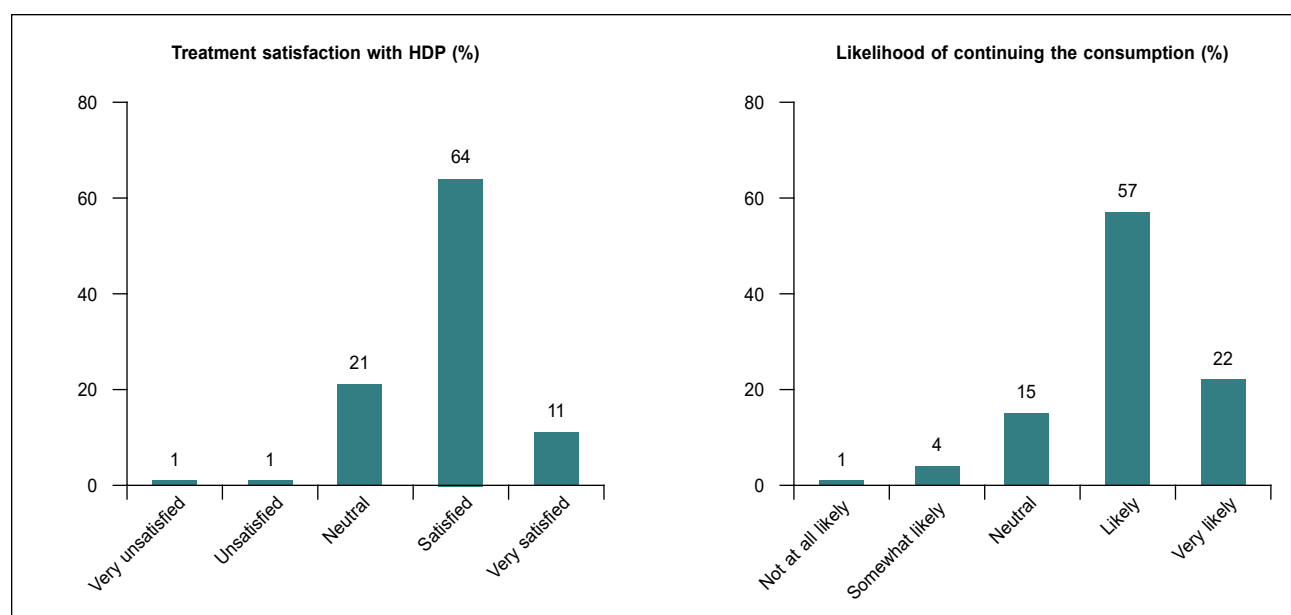


Figure 1. Treatment satisfaction and likelihood, HDP group

Table 4. Consumption of Fiber per Day and Nutritional Supplements in HDP Group

Quantity	n (%)	Frequency	n (%)
1 leveled scoop (<30 g)	634 (41.76)	Once a day	411 (64.82)
		Twice a day	215 (33.91)
		NR	8 (1.26)
2 leveled scoops (30 g)	868 (57.18)	Once a day	742 (85.48)
		Twice a day	121 (13.94)
		NR	5 (0.57)

Satisfaction and likelihood of continuing the consumption of HDP

In the HDP group, 75% of patients were satisfied or very satisfied with the HDP product; nearly 80% of patients reported that they were very likely-likely to continue consuming it and 79% of patients reported high compliance (likely + very likely) with HDP (Fig. 1). About 41.76% of patients consumed <30 g of the HDP product once or twice a day, while 57.18% consumed 30 g once or twice a day (Table 4).

DISCUSSION

The results of our surveys showed that all physicians were aware of the importance of dietary fiber in managing glycemic parameters, weight and cholesterol and prescribed fiber-rich nutritional supplements to their patients with T2DM. However, they reported a

lack of awareness among patients with T2DM about the importance of fiber and that patients consume less than the recommended amount of fiber. In the patients' survey it was found that two-thirds of patients who were not taking HDP supplement were aware about the benefits of high-fiber diet, though this proportion was >90% in those taking the supplement. Patients consuming HDP supplement reported an improvement in HbA1c as well as weight loss 3 months after initiating HDP. In both surveys, increased energy levels and satiety were reported to be the main benefits of consuming HDP. The compliance to HDP was good.

A high-fiber diet is known to reduce total cholesterol and LDL cholesterol.²⁶ A high intake of soluble dietary fiber above the ADA recommended level, was shown to decrease blood glucose, insulin and serum lipid levels in a study.²⁷ In another study among urban Indians with T2DM, patients with low consumption of dietary fiber (<29 g/day) had higher prevalence of hypercholesterolemia and higher LDL than patients with median consumption of fibers.²⁸ One more study among diabetic patients in India showed a significant reduction in serum cholesterol with a high-fiber diet and this was sustained over a prolonged period.²⁹ In a systematic review, Reynolds et al reported the outcomes of 27 trials about increasing fiber intakes on total cholesterol. Increased fiber intake resulted in reduction of total cholesterol, LDL cholesterol and triglycerides. There were no differences by diabetes type, therapy, risk of bias, fiber type, trial size or trial duration. Similarly, increasing the fiber intake reduced body weight by

a mean of 0.56 kg, BMI by a mean of 0.36 kg/m² and waist circumference by a mean of 1.42 cm, despite no recommendations for reduction in calorie intake.³⁰ Water-soluble fibers are most effective in reducing LDL cholesterol, though they do not considerably affect high-density lipoprotein (HDL) levels.²⁵

Studies have also shown a decrease in glycemic parameters with a high-fiber diet. A recent systematic review and meta-analysis of 28 randomized controlled trials (RCTs) assessed the effect of viscous fiber intake in patients with T2DM. There was an absolute decrease of 0.58% in HbA1c and 0.82 mmol/L in fasting blood glucose following a median dose of 13.1 g/day for a median duration of 8 weeks. Patients with higher baseline HbA1c showed greater reductions.³¹ Silva et al analyzed 12 RCTs and reported a decrease of 0.52% in HbA1c and 0.55 mmol/L in fasting blood glucose following a high intake of various types of soluble and insoluble dietary fiber.³² Another meta-analysis of 19 studies reported that the multivariable-adjusted risk of T2DM decreased significantly by 9% for every 10 g/day increase in intake of total dietary fiber.³³ There is a major difference between Asians and Caucasians in the postprandial β -cell response to glucose.³⁴ T2DM in East Asians is characterized primarily by β -cell dysfunction rather than IR.³⁵ Dietary fiber reduces carbohydrate absorption in the small intestine³⁶ and thus prevents a rapid rise of blood glucose levels, which is important in the East Asian population with limited insulin secretion capacity.³⁷ Indian meals often consist of high-calorie foods that are high in processed carbohydrates and saturated fats. These cause a significant increase in postprandial blood glucose, free fatty acids and triglycerides, leading to higher CVD risk.³⁸ In a recent study among Indian patients, ingestion of a fiber-rich nutritional supplement containing nutriose and fibersol in the form of a drink, significantly reduced the postprandial blood glucose peak following a high-fat meal in overweight subjects with impaired fasting glucose.³⁸

While insoluble fiber is more helpful for colonic health and increasing the stool bulk, viscous fibers have pleiotropic metabolic effects.³⁹ HDP contains nutriose and fibersol. Nutriose is a wheat fiber dextrin with clinically proven digestive tolerance, while fibersol is a corn fiber dextrin that is digestion resistant, a low-calorie soluble fiber and bulking agent.³⁸ Fiber intake of >50 g/day is difficult to achieve without the use of dietary fiber supplements.⁴⁰ Although it is preferable to meet the daily fiber requirement through food rather than supplement, the use of the latter makes it easier to

measure and achieve the goal of daily fiber requirement despite lack of willingness or ability to modify the diet.⁴¹ Moreover, as seen in our survey, most patients were willing to take the supplement if recommended by the physician. Further, the compliance among those prescribed the supplement was very high. Hence, increasing the awareness about the importance of fiber-rich food along with prescription of a fiber-rich supplement, if necessary, might lead to an overall increase in the intake of fiber per day among patients with T2DM.

There were certain limitations to our survey. The first is that the HbA1c and blood glucose values as well as weight were based on patients' recall from memory and the actual reports were not checked as a part of the survey. Hence, there is a likelihood of recall bias, which can lead to an over or under estimation of reported values. Second, the compliance was also self-reported and not actually monitored as this was not a clinical trial. Nevertheless, this is the first survey to assess the subjective and objective outcomes following a high-fiber supplement consumption among Indian patients with T2DM. Findings from this survey can be further evaluated and supported by conducting large multicenter real-world clinical evidence studies pan India.

CONCLUSION

The results of our survey show a high level of awareness among physicians about the importance of a high-fiber diet in patients with T2DM and recommendations about the same to patients. Patient awareness about the same needs to be increased. Nevertheless, there was a high level of acceptance and compliance to take high-fiber supplements if recommended by physicians. The main benefits of HDP as a fiber supplement were decrease in HbA1c and weight and an increase in satiety and energy levels.

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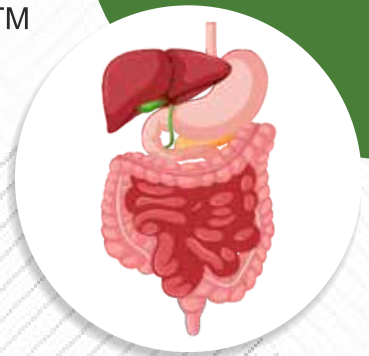
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A Survey to Assess the Efficacy and Tolerability of Natural Appetite Stimulants in Pediatric Patients

DURGAPRASAD MARATHE*, PRADYUMNA RATNAKAR†

ABSTRACT

Anorexia, a common symptom in children, leads to undernutrition, with over 60 million underweight children in India suffering from frequent illnesses. Lack of adequate diet, proper breastfeeding and sufficient protein contribute to increased incidence of undernutrition. Parents often complain their children don't eat enough, making mealtimes difficult and impeding growth. Appetite stimulants like cyproheptadine are available, but side effects like sedation, fatigue, disorientation, impaired coordination, restlessness, excitation and irritability limit their use especially in the pediatric population. The use of herbal supplements has increased worldwide, with parents seeking guidance from pediatricians and primary care professionals regarding the efficacy and safety of these products. The study was a retrospective study conducted via a questionnaire-based survey among all doctors between April and June 2023 to assess the efficacy and tolerability of natural appetite stimulants in pediatric patients. Results showed that patients in the age group of 0 to 5 years (23.1%) were the most common visitors in the doctor's clinic and appetite stimulant agents were being prescribed most of the time (44.8%). They preferred prescribing natural appetite stimulant mostly (34.3%) for poor appetite (37.3%), followed by poor weight gain and growth (22.8%). The natural appetizer was found to be nonaddictive and nonsedative with an improvement in the overall well-being (31.3%) among patients. The results suggest that the natural intervention has the potential to serve as a valuable adjunctive therapy in managing appetite challenges and promoting healthy weight gain in pediatric populations and to optimize pediatric nutrition and overall well-being.

Keywords: Anorexia, undernutrition, natural appetizers, efficacy, tolerability, children

Pediatric patients facing appetite challenges often pose a significant concern for health care professionals and caregivers. Limited food intake can lead to undernutrition, inadequate growth and diminished overall health. A loss of appetite can weaken the immunity and the body becomes susceptible to different infections, which might become life-threatening.¹

Consequently, the need to explore safe and effective appetite stimulation methods becomes paramount. Several appetite stimulants are available, one of which is cyproheptadine. Drowsiness and somnolence were the most frequently reported side effects of using

cyproheptadine. So far 1 case of acute liver failure has also been documented after use of cyproheptadine.^{2,3}

Phytochemicals derived from plants have been reported to be well-tolerated by the human body and hence increasingly being used as effective therapeutic alternatives against various illnesses, including viral infections. According to a study, from 1940 to 2014, 49% of all small molecules approved by the US Food and Drug Administration (FDA) were natural products or their derivatives.⁴

In recent years, the use of natural appetite stimulants has gained attention as a potential solution for pediatric patients. These natural substances, derived from herbs, plants or other organic sources, are believed to possess properties that can enhance appetite and support healthy weight gain.

Herbs that significantly increase appetite include Guduchi, Saunf, Kutki, Vidang, Amalaki, Kachur, Yavani, Pippali, Jeera and Nagarmotha. They have strong immunomodulatory, antidiabetic, antispasmodic,

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CLINICAL STUDY

anti-inflammatory, antioxidant, antistress and hepato-protective qualities. These properties work in concert to enhance digestion and lessen digestion-related issues including diarrhea, colitis, vomiting, hyperacidity, etc.⁵⁻¹⁸

However, despite their widespread use, the efficacy and tolerability of these natural appetite stimulants in pediatric patients remain largely anecdotal and poorly understood.

To bridge this knowledge gap, a questionnaire-based survey is presented here; it is designed to assess the effectiveness and tolerability of natural appetite stimulants in pediatric patients. By capturing the firsthand experiences and opinions of health care professionals, caregivers and the patients themselves, this survey aims to provide valuable insights into the practical use and outcomes of these natural interventions.

METHODS

Study Design and Setting

The study was a retrospective study conducted via a questionnaire-based survey among all doctors between April and June 2023. It is a mixed-method study to assess the efficacy and tolerability of natural appetite stimulants in pediatric patients.

Study Population

All qualified doctors (General Practitioners, Physicians and Pediatricians) practicing modern medicine were eligible for the survey and were approached to participate. The survey intended to include doctors across all clinical departments, work experience and professional hierarchy to ensure the representation of different specializations.

In this study, 3325 Indian doctors participated in the questionnaire survey on treatment options for loss of appetite and poor immunity among children, starting from infants.

Data Collection

The survey tool was a validated questionnaire containing 11 questions. It was in the form of a closed-ended questionnaire, was developed by an expert panel comprising a physician, and a pharmacologist. The questionnaire was specifically focused on the study aims and tailored contextually to fit local situations.

All filled forms were entered into the software database. For discrepancies related to data entry alternate forms were physically cross-checked. Complete cases were analyzed and missing data were not included because of

low occurrence. The data were analyzed after cleaning the data and final report was prepared.

RESULTS

In the study, patients in the age group of 0 to 5 years (23.1%) were the most common visitors in the doctor's clinic followed by those who were 6 to 10 years old (19.5%) and 8.8% children who were more than 10 years visited by doctors minimum as depicted in Figure 1.

It was further observed that doctors prescribed appetite stimulant agents to their patients most of the time as is shown in Figure 2 and 47.1% are aware that there are natural appetite stimulants available in the market (Fig. 3).

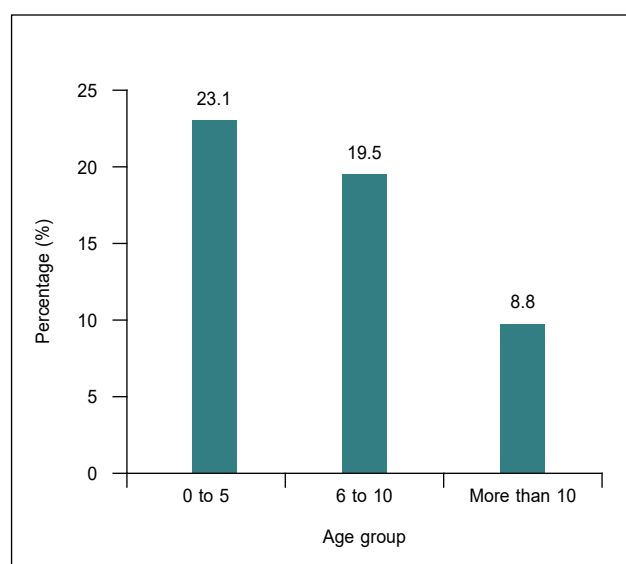


Figure 1. Graph showing patient age group visiting doctors.

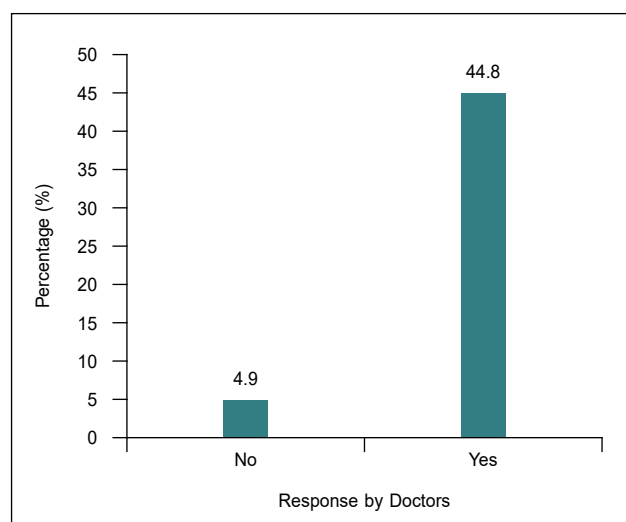


Figure 2. Graph showing doctors response in prescribing appetite stimulant agents.

Figure 4 shows the graph depicting the preference of doctors for the natural appetite stimulant mostly (34.3%) containing a natural combination of ingredients like Saunf + Guduchi + Amalaki + Kutki + Vidang.

Figure 5 shows graph depicting major side effects of appetite stimulants such as cyproheptadine which included drowsiness (30.3%), dizziness (18.6%), dry mouth, nose and throat (9.8%), followed by nausea (7%), muscle weakness (6%) and excitement (2.2%).

The study survey found that mostly doctors prescribed natural appetizer for poor appetite (37.3%), followed by poor weight gain and growth (22.8%), and followed

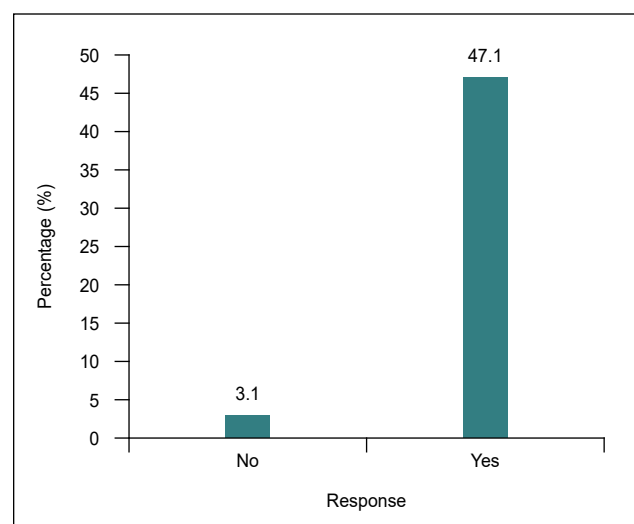


Figure 3. Graph showing awareness of doctors about availability of natural appetizers in the market.

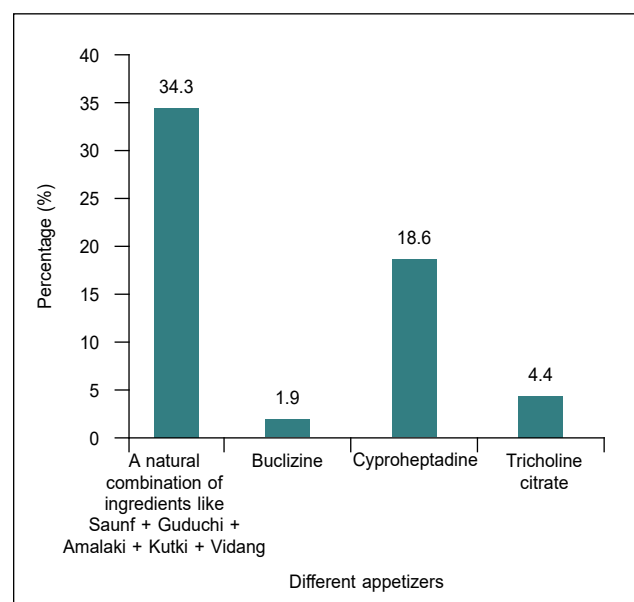


Figure 4. Graph showing preference of doctors for the natural appetizers.

by poor immunity (9%) and constipation (5.5%) as is evident from the Figure 6.

Intake of natural appetizer showed 31.3% improvement in overall well-being which included improvement in food intake, energy levels and satiety with additional features of being nonaddictive and nonsedative as shown in Figure 7.

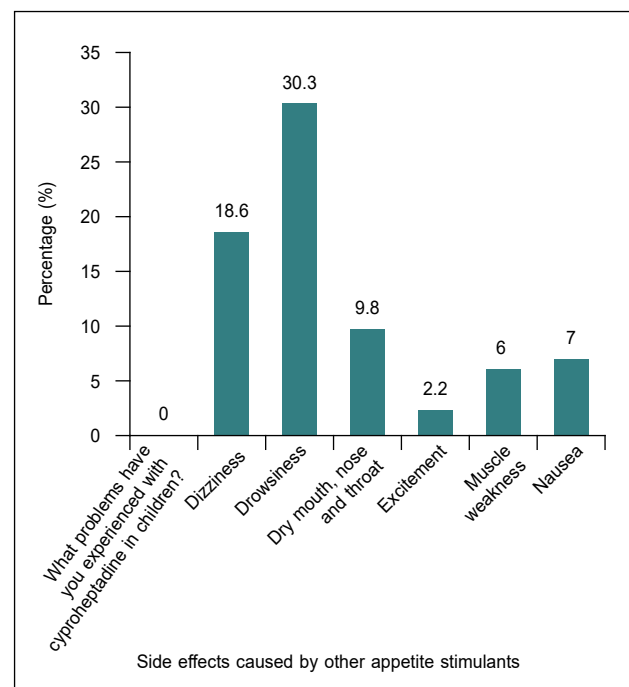


Figure 5. Graph showing major side effects of appetite stimulants such as cyproheptadine.

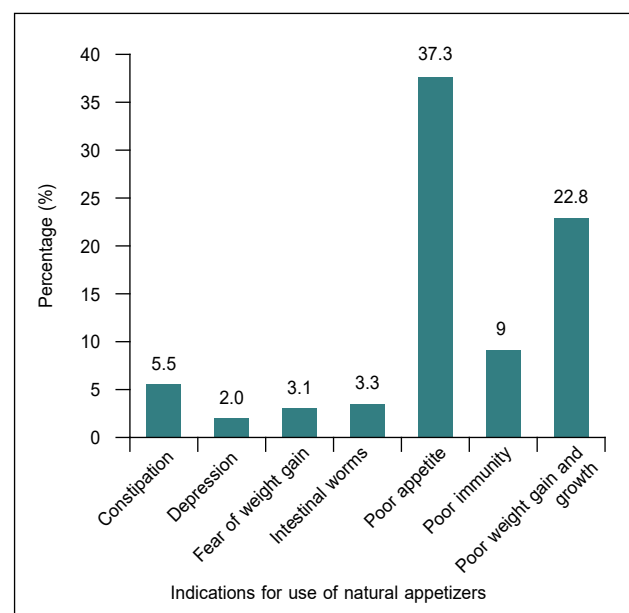


Figure 6. Graph showing indications for use of natural appetizers.

CLINICAL STUDY

The majority of natural appetizers exhibited superior natural appetite stimulant, digestive and carminative characteristics with strong orexigenic nature and ideal growth among children. It was also discovered to be safer than cyproheptadine because they don't have the typical adverse effects of cyproheptadine. The advantages or beneficial properties of the natural appetizer are evident from the Figure 8.

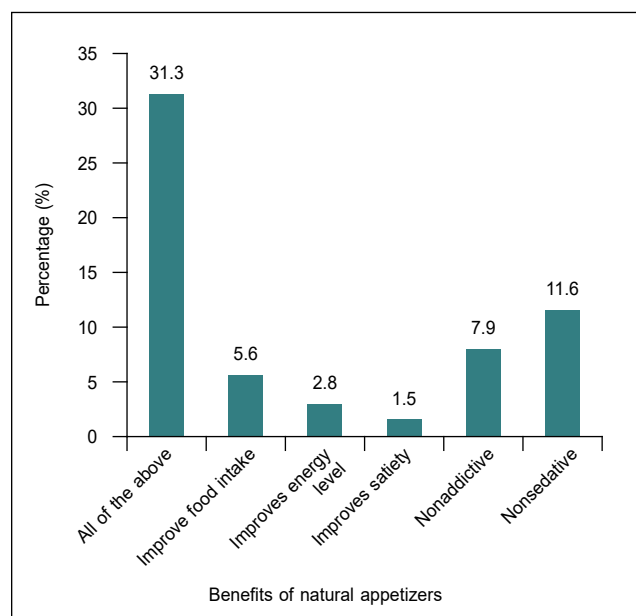


Figure 7. Graph showing benefits of using natural appetizers.

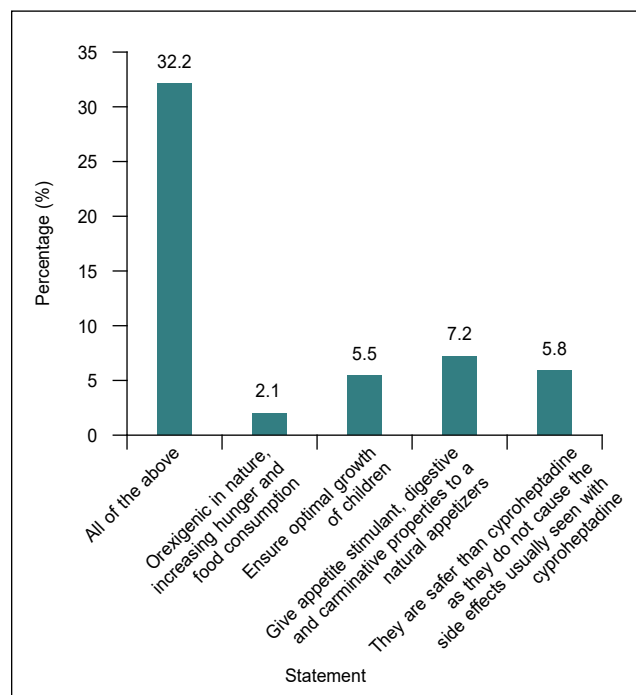


Figure 8. Graph showing beneficial properties of using natural appetizer.

In the study Figure 9 showed that natural appetizers discussed herein did not show common side such as chest congestion, drowsiness, headache, low energy levels and nausea which is mostly observed in others, which emphasizes the better safety and tolerability profile of the natural appetizer.

Further, the results as depicted in Figure 10, showed that the discussed natural appetizers showed better compliance (36.4%). Hence, the natural appetizer is having better safety and tolerability profile. Patients who reported compliance problems said that reason was mostly related to resistance to taking medicines, not tasty and forgetting to time, etc.

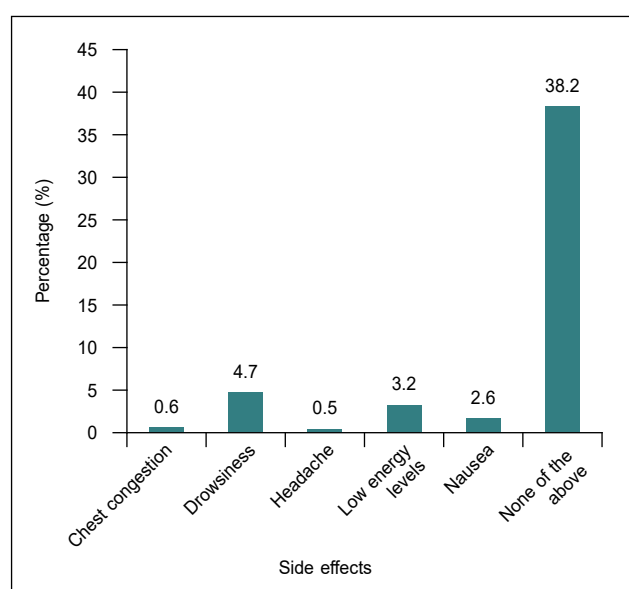


Figure 9. Graph showing better safety tolerability profile of the natural appetizer.

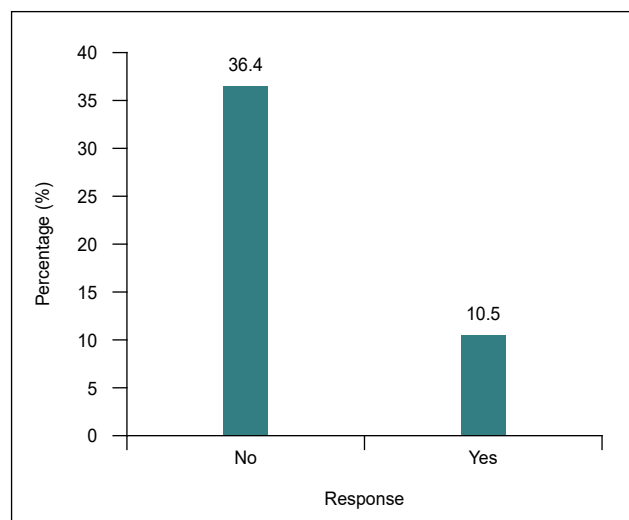


Figure 10. Graph showing response to experiences of any compliance problems with natural appetizer.

DISCUSSION

The present perception-based survey aimed to assess the efficacy and tolerability of a natural appetite stimulant containing Guduchi, Saunf, Kutki, Vidang, Amalaki, Kachur, Yavani, Pippali, Jeera and Nagarmotha in pediatric patients. Through the collection of subjective experiences and opinions from health care professionals, caregivers and the patients themselves, we sought to gain insights into the practical use and outcomes of this particular natural intervention.

Guduchi (*Tinospora cordifolia*) has a wide variety of compounds that may have physiological effects. It is reported to offer exceptional immunomodulatory, anti-diabetic, antispasmodic, anti-inflammatory, antioxidant, antistress and hepatoprotective effects, which combined enhance digestion and lessen digestion-related issues including diarrhea, colitis, vomiting, hyperacidity, etc.⁵

Fennel, or *Foeniculum vulgare* (Apiaceae), is a well-known and significant medicinal and fragrant plant used to treat digestive, gastrointestinal and carminative problems. It is believed that *F. vulgare*'s phenolic components are what give its antioxidant and hepatoprotective properties.⁶

A number of studies revealed that *F. vulgare* is useful in treating a variety of diseases, such as abdominal pains, colic in children, conjunctivitis, constipation, detoxifying, diarrhea, flatulence, gastralgia, gastritis, irritable colon, kidney problems, laxative, leukorrhea, liver pain, mouth ulcer and stomachache.⁷

Embelia ribes, often known as Robustal Berries or Vidanga, is a natural germicide. Its medicinal uses, health advantages and effectiveness in treating elephantiasis, children who grind their teeth while they sleep, stomach worms, heart conditions, facial paralysis caused by heat exhaustion, blood motions, sticky motions, back pain during periods, eye brow pains, forehead pains and blood motions. Children's appetites are improved when they consume 3 g of *E. ribes* powder twice daily together with honey. This remedy treats all issues brought on by stomach worms.^{8,9}

Kutki (*Picrorhiza kurroa*) has been recommended for a variety of clinical conditions, including anorexia, burning sensation, fever, intermittent fevers, prediabetic and diabetic states, asthma, cough, helminthiasis, adipolysis, orexigenic, laxative, anti-inflammatory, hepatoprotective and diuretic activities. It is also beneficial for heart function and hepatobiliary and gastrointestinal disorders. As a result, it becomes a good option for natural appetite stimulant number.¹⁰

The *Embllica officinalis* fruit is astringent in character and primarily composed of tannins, which have a significant potential for treating digestive illnesses like diarrhea and dysentery. It works well to reduce hyperacidity.¹¹

Cyperus rotundus L., also known as Nagarmotha, is frequently used to treat a wide range of conditions and illnesses, including indigestion, constipation, dysentery, abdominal distention, neurogenic gastralgia, chest pains, painful and irregular catamenia, skin conditions, furuncle infections, staphylococcal infections, leprosy, sprains and bruises, fever and stomach pain from animal tissue. It possesses a wide range of pharmacological qualities, including antibacterial and microbial activity, gastrointestinal activity, anti-inflammatory, antilaceration, wound healing activity, insecticidal properties, antioxidant, antiobesity, antidiarrheal activity, antiseptic activity and antipyretic activity. It is also nutritionally beneficial. Hence including this in a natural appetite stimulant enhances the property.¹²

Extracts from the roots and fruits of *Piper longum* contains several bioactive phytochemicals and essential oils were found to have a number of pharmacological benefits, including antimicrobial, antiparasitic, anthelmintic, antioxidant, anticancer, hepatoprotective, anti-angiogenic, immunomodulatory and so forth. Ayurvedic medication considers *P. longum* as a potent rejuvenator and is effective and helpful in treating bloating and flatulence.^{13,14}

Cumin (*Cuminum cyminum*) extracts have been demonstrated in studies to have greater protease, lipase and amylase activities, suggesting a potential function in boosting the digestive enzymatic activities. These extracts improve phytase activity, which increases the bioavailability of minerals and improves digestion and appetite.¹⁵

Trachyspermum ammi, also known as "Ajwain" increases gastric acid secretion. Tests on anesthetized rat revealed that *T. ammi* causes a nearly fourfold increase in gastric acid production. *T. ammi* was added to the diet of experimental rats *in vivo*, where it decreased food transit time, increased the activity of digestive enzymes, and/or increased bile acid secretion.^{16,17}

Curcuma zedoaria has been found to have anti-inflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, antidiabetic, antibacterial, antifungal, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, hypotensive and hypocholesteremic properties. It demonstrated exceptional natural antibacterial, disinfecting, anti-inflammatory and analgesic effects.

It also aided digestion to enhance gut flora. Bloating, indigestion and intestinal worm infestation has been treated with it since long time.¹⁸

Thus the ingredients present in the natural appetite stimulant discussed here seem to have several beneficial effects on the body, enhance immunity and overall health. The survey results indicated a generally positive perception regarding the efficacy of the natural appetite stimulant in pediatric patients.

A significant number of health care professionals and caregivers reported observing improvements in appetite and food intake among the patients who received this intervention. Figure 2 showed doctors prescribed appetite stimulant agents to their patients most of the time (44.8%) and 47.1% were aware of that natural appetite stimulants are available in the market (Fig. 3). Figure 4 (34.3%) showed that the use of natural appetizer was more prevalent. Figure 6 demonstrated that mostly doctors prescribed natural appetizer for poor appetite (37.3%), followed by poor weight gain and growth (22.8%) and followed by poor immunity (9%) and constipation (5.5%).

Figure 5 shows that mostly pediatric patients complained of drowsiness and dizziness after taking cyproheptadine as an appetite stimulant. Several appetite stimulants are available, one of which is cyproheptadine, but commonly reported side effects such as drowsiness and somnolence limits its use.²

In a case study reported by Chertoff et al, a 55-year-old white female without a history of liver or gastrointestinal disease was admitted with acute liver failure after trying cyproheptadine for increasing appetite. Treatment involved supportive care, symptomatic medication and discontinuation of cyproheptadine. The authors also stated that in more than 20 years, this is the only case of cyproheptadine-induced acute liver failure that has been documented.³ Figure 7 shows the beneficial effects of the natural appetizer compared to other appetizer. Benefits included improvement in food intake, improvement energy levels and satiety with additional features of being nonaddictive and nonsedative.

The majority of respondents expressed that the natural ingredients within the appetite stimulant appeared to have a positive impact on increasing the desire to eat and promoting healthy weight gain in pediatric patients. They stated that natural appetizer containing Guduchi, Saunf, Kutki, Amalaki, Nagarmotha, Jeera, Pippali, Yavani, Kachur and Vidang exhibited better natural appetite stimulant, digestive and carminative properties with profound orexigenic nature and optimal growth

of children. It was additionally found to be safer than cyproheptadine as they do not cause the side effects usually seen with cyproheptadine. The benefits of the natural appetizer are evident from the Figure 8.

Furthermore, the survey responses revealed that a considerable proportion of pediatric patients themselves reported experiencing an enhanced appetite and an increased interest in food after using the natural appetite stimulant.

In terms of tolerability, the survey findings highlighted that the natural appetite stimulant was generally well-tolerated by pediatric patients. Both health care professionals and caregivers reported minimal adverse effects associated with the use of this intervention. Figure 9 showed that common side effects mostly observed by other appetite stimulants were not observed in the natural appetizer. Further, the results showed that natural appetizer had a better compliance among the patients (36.4%, Fig. 10) and hence these were safe alternatives.

IMPLICATIONS AND LIMITATIONS

The results of this perception-based survey hold important implications for pediatric health care practice and nutrition management.

However, it is important to acknowledge certain limitations of this survey. Firstly, the study relied on subjective perceptions and self-reported experiences, which may introduce biases and variations in responses. Additionally, the survey did not include a control group or comparative analysis, making it difficult to establish a direct causal relationship between the natural appetite stimulant and observed improvements in appetite.

Hence, more research endeavors should focus on conducting controlled clinical trials to validate the findings of this perception-based survey. Such trials could include different parameters like dietary intake, and nutritional status to provide more robust evidence of the efficacy and tolerability of the natural appetite stimulant in pediatric patients.

CONCLUSION

To conclude the perception-based study on the effectiveness and acceptability conducted on pediatric patients showed an overall favorable opinion regarding its efficacy and tolerability of a natural appetite stimulant including Guduchi, Saunf, Kutki, Vidang and Amalaki, Pippali, Jeera, Yavani, Kachur and Nagarmotha. The results suggest that this natural intervention has the

potential to serve as a valuable adjunctive therapy in managing appetite challenges and promoting healthy weight gain in pediatric populations.

These findings can help health care professionals and caregivers to make more informed decisions regarding the use of natural appetite stimulants to optimize pediatric nutrition and overall well-being.

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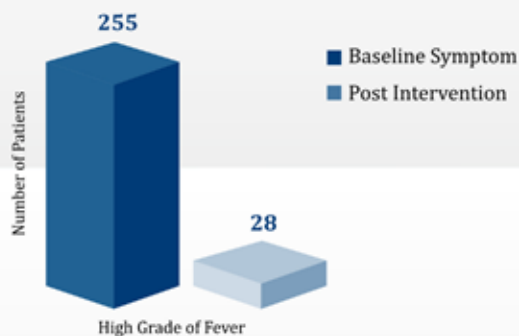


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- Effective resolution of Pain seen on VAS score¹
- Significant analgesia observed at the site of injection²

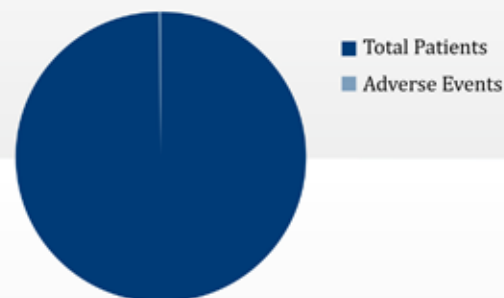
Patient Response after Paracetamol + Lignocaine Injection

- 89% patients showed resolution of Fever¹
- It was well tolerated in 99.7% patients, proves overall safety of this combination.¹

Efficacy of Paracetamol + lignocaine combination



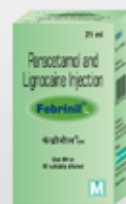
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2. HayatM, Afshan G, Nasir M, AsgharS, Monem M. 2020 Feb,10 (cited 2022 Jan21); 12 (2)

Safety and Efficacy of Paracetamol + Lignocaine Injection in Patients with High-grade Fever: A Prospective Analysis

SANDIPANI NAYAK*, P SHAILESH†, ARUN PAHARIA‡, KRISHANU KRORI#, SHIBSANKAR PAL‡

ABSTRACT

High-grade fever is a common presenting symptom in various infectious and inflammatory conditions, requiring prompt and effective management. Paracetamol (acetaminophen) is a widely used antipyretic agent, while lignocaine possesses analgesic and anti-inflammatory properties. This prospective study evaluated and established the safety and efficacy of paracetamol + lignocaine injection in patients with high-grade fever. The study outcomes revealed that after administering paracetamol and lignocaine injections, 89% of patients experienced a reduction in high fever, while 68.6% of patients reported no or mild pain at the injection site. Based on these findings, the authors recommend that health care professionals consider the potential benefits of using paracetamol and lignocaine injections for patients suffering from severe fever accompanied by pain and discomfort.

Keywords: Fever, antipyretic, analgesic, anti-inflammatory

BACKGROUND

Elevated body temperature exceeding 38.3°C (100.4°F), known as fever, is a commonly observed abnormal physical sign in ill patients, often associated with systemic inflammatory response syndrome (SIRS) or infections. Fever has been linked to prolonged hospital stays in general intensive care unit (ICU) patients and unfavorable outcomes in specific patient populations.¹ To address fever, antipyretic therapy is typically initiated, which involves administering antipyretic medications or applying external cooling methods. The primary rationale behind such interventions includes enhancing patient comfort, reducing cardiovascular strain and preventing excessive oxygen consumption.¹ Prompt management of fever alleviates patient

discomfort, minimizes complications and optimizes patient outcomes.²

In clinical settings (community health care settings and hospitals), fever is frequently managed by administering acetaminophen (paracetamol) to reduce body temperature. Even in the ICU, using acetaminophen to treat fever in patients with infection is a common practice, driven by the rationale that fever places additional physiological stress on patients who are already critically ill.³

Additionally, lignocaine is also famed for its analgesic, anesthetic and anti-inflammatory properties,⁴ which can effectively reduce pain at the injection site and improve patient compliance. The combination of paracetamol and lignocaine has emerged as a promising therapeutic option owing to their complementary pharmacological properties.⁵

Given the significance of effective fever management in patients with high temperatures, it is crucial to examine the safety and efficacy of acetaminophen injection as a treatment for high fever.³

AIM

This study aims to evaluate the outcomes surrounding the administration of paracetamol + lignocaine injection in patients with high-grade fever. This research aims to provide insights into the safety and effectiveness

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CLINICAL STUDY

associated with this common practice by analyzing the obtained data.

METHODS

The study included:

- Patients who were 18 years or older.
- Experiencing high-grade fever ($>102^{\circ}\text{F}$).

Patients with serious underlying conditions such as acquired immunodeficiency syndrome (AIDS), cancer and renal or hepatic dysfunction were excluded.

Upon enrollment, the patients underwent measurement of initial body temperature and documented any associated symptoms. The patients received either intravenous (IV) or intramuscular (IM) administration of paracetamol + lignocaine injection, and their feedback regarding pain score (at the injection site) was recorded using a visual analog scale (VAS). Temperature readings and observations of any changes in associated symptoms were noted 15 to 30 minutes after administration. The occurrence of side effects, such as skin rashes, nausea, vomiting, etc., was monitored in the patients.

Written consent was obtained from all participants after providing them with comprehensive information about the study, the use of the medication in their condition, and the potential side effects. Data were collected anonymously, and the responses were analyzed using simple percentage calculations.

RESULTS

The study sample consisted of 349 patients, with 160 females and 189 males. Two hundred fifty-five patients initially presented with a baseline fever exceeding 102°F , while all the participants had some degree of fever. Among all the enrolled patients, 320 reported pain as an associated symptom, including 12 patients with joint pain, 6 with associated injury and 1 with severe arthralgia, abdominal pain and chest pain.

Following the administration of parenteral paracetamol + lignocaine injection, within a span of 30 minutes, 89% of patients experienced a reduction in high fever. Notably, 68.6% of patients reported no or only mild pain at the injection site (based on VAS score). Figure 1 depicts the baseline and post-intervention data of the patients regarding the efficacy of paracetamol + lignocaine injection in terms of fever resolution.

Furthermore, the parenteral administration of paracetamol + lignocaine injection demonstrated excellent

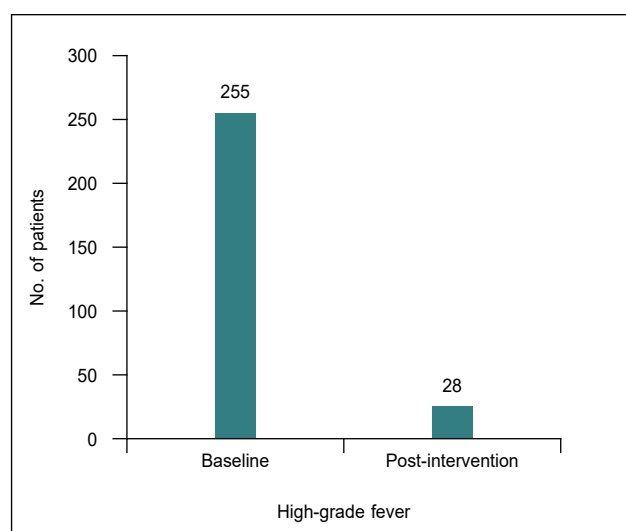


Figure 1. The reduction in the number of fever patients post-intervention.

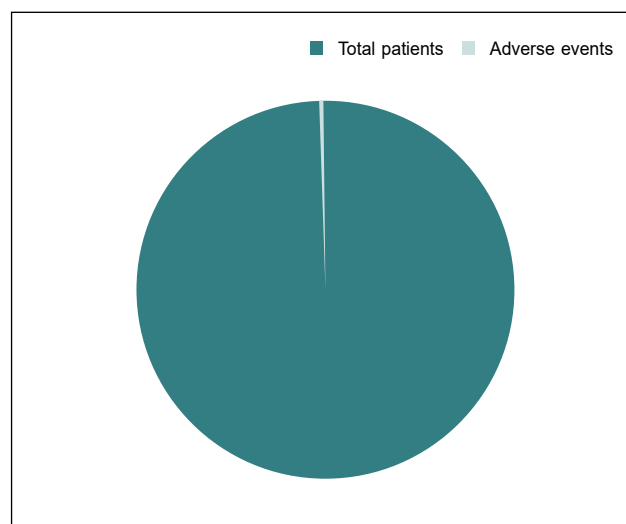


Figure 2. The post-intervention data regarding the safety of paracetamol + lignocaine combination.

tolerance in 99.7% of the patients, which proves the safety of this combination. Figure 2 depicts the post-intervention data of the patients regarding its safety.

These observations highlight the positive impact of the parenteral paracetamol + lignocaine combination in managing fever and pain in patients with high-grade fever.

DISCUSSION

Paracetamol (acetaminophen) is unquestionably a highly prevalent medication utilized globally. As an easily accessible over-the-counter drug, paracetamol is widely recognized as the primary and initial choice for treating fever and acute pain.⁶

Young et al in 2015 evaluated the effectiveness of acetaminophen in managing fever and probable infection and found that patients who received acetaminophen exhibited a lower mean daily peak body temperature, a lower mean daily average body temperature, and sustained resolution of fever compared to the placebo group. They also found that the occurrence of adverse events was not significantly different between the acetaminophen group and the placebo group. Overall, these findings demonstrate a modest antipyretic effect of parenteral paracetamol (acetaminophen) in patients with fever and probable infection.³ These findings align with our study as most of the patients (89%) receiving paracetamol + lignocaine injection experienced sustained resolution of fever without any adverse effects.

The combination of lignocaine and paracetamol is highly effective in reducing pain at the injection site and improving patient compliance. Recent studies have demonstrated that when lignocaine is administered alongside IV paracetamol, the occurrence of pain is dramatically reduced to a mere 2%, thereby increasing the overall acceptance of this particular formulation among patients.⁷ This result is even evident in our study, where paracetamol + lignocaine injection significantly decreased the pain at the injection site, as evident by the lowered VAS scores in the majority of the patients (68.6%).

Furthermore, clinical studies have shown a high level of tolerability, with extremely rare adverse reactions,⁸ which is also evident in our study and thus proves parenteral paracetamol to be desirable and safe.

CONCLUSION

Our study highlights the effectiveness of IV administration of a combination of paracetamol and lignocaine, which results in a rapid onset of action within 15 to 30 minutes. This treatment approach offers several favorable outcomes, including the absence of adverse effects, effective reduction of associated signs and a prolonged duration of action. Paracetamol + lignocaine injection ensures painless administration at the injection site, which enhances convenience for health care professionals. This injection's dual mechanism of action provides both antipyretic and analgesic benefits, making it a valuable choice for fever management.

These findings support the clinical rationale of utilizing paracetamol + lignocaine injection for short term

management of moderate pain and fever. It is recommended that physicians consider integrating this approach into their patient care strategies for individuals experiencing fever and related discomfort or pain.

Indian studies prove the safety and efficacy of a fixed-dose combination of paracetamol and lignocaine in managing high-grade fever and pain.

The combination of paracetamol and lignocaine:

- Is entirely safe when administered through the IM or IV route in patients.
- Effectively reduce pain at the injection site, as evidenced by a favorable VAS score.
- Significantly decreases body temperature in most patients indicating the effectiveness of the paracetamol and lignocaine combination.

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An Investigation of the Equivocal Relationship Between Daydreaming, Creativity and Well-Being

RIDDHIMA KAMAT*, JOSEPH M DIEHL†

ABSTRACT

An extensive number of studies have been conducted on the relationship between daydreaming, creativity and well-being, with mixed results, nonetheless. Particularly, research has demonstrated both positive and negative effects of daydreaming on creativity and well-being, as well as of creativity on well-being. In addition, most studies have been conducted on adults. Therefore, the purpose of this survey-based study conducted in, Delhi University in May 2023 was to further explore the relationship among the aforesaid constructs on a sample of late adolescents. To this aim, 622 Indian were asked to complete three psychometrically validated scales. The following research hypotheses were proposed: H1) Daydreaming would be a statistically significant predictor of creativity; H2) Daydreaming would be a statistically significant predictor of overall distress, stress, anxiety and depression; H3) There would be a statistically significant difference in daydreaming among severity levels of stress, anxiety and depression; H4) Creativity would be a statistically significant predictor of overall distress, stress, anxiety and depression; and H5) There would be a statistically significant difference in creativity among severity levels of stress, anxiety and depression. Results showed that daydreaming was not a statistically significant predictor of creativity, but greater daydreaming was related to higher distress, stress, anxiety and depression. Furthermore, participants with higher creativity experienced greater anxiety. Nevertheless, creativity was not a statistically significant predictor of distress, stress and depression. Finally, participants with extremely severe depression displayed lower creativity than those with moderate depression. Further research is advised before practical implications are recommended.

Keywords: Daydreaming, stress, anxiety, late adolescents

Daydreaming can be defined as thoughts and images emerging when attention shifts from external tasks to a private, internal flow of consciousness.¹ According to the extensive research of Singer on daydreaming, three styles of daydreaming can be identified: positive constructive daydreaming (i.e., playful-wishful imagery and resourceful-creative thought), guilty-dysphoric daydreaming (i.e., obsessive, distressful fantasies) and poor attentional control (lack of ability to focus on current thought or task).² Based on this classification, studies have explored the benefits of daydreaming, as well as its relationship with rumination, mood and cognitive failure.³

To elaborate, a large body of research has investigated the impact of daydreaming on creativity with seemingly

contradictory findings. Particularly, it has been observed that daydreaming can boost overall creativity⁴ or creativity after a demanding activity⁵ and lead to spontaneous insights.⁶ However, other studies portrayed daydreaming as a source of distraction,³ with individuals rarely considering daydreaming to be pleasurable.⁷ In addition, it has been suggested that mindful awareness enhances more creativity than daydreaming⁸ and that daydreaming may be indirectly related to creativity through individual differences.⁹ Nevertheless, it has been argued that a distinction between different types of daydreaming and creativity should be made for accurate conclusions to be drawn, as different types of daydreaming benefit different types of creativity.^{10,11}

In the same vein, mixed findings have been reported on the relationship between daydreaming and well-being. In further detail, it has been demonstrated that daydreaming can promote well-being through adaptive emotion regulation¹² and distancing oneself from stressful situations.¹³ On the other hand, Killingsworth and Gilbert based on their research on daydreaming and positive feelings, concluded that a “*wandering mind is an unhappy mind*”.¹⁴ However, as in the case of

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daydreaming and creativity, it has been proposed that the impact of daydreaming on mood is dependent on the content of daydreaming, with positive constructive daydreaming being related to personal growth and positive affect and guilty-dysphoric daydreaming being associated to negative affect, lower well-being and depressive symptoms.¹⁵

Finally, the relationship between creativity and well-being is another topic that has sparked research interest. Specifically, it has been documented that creativity promotes psychological well-being¹⁶ and can act as a protective against psychopathology¹⁷. Also, a meta-analysis of 32 studies with a total sample of approximately 8,000 individuals concluded that creativity is positively related to well-being and that past links between creativity and psychopathology (the mad-genius hypothesis) are most likely applicable to clinical levels of psychopathology. Also, it was argued that the direction of the relationship differentiates between the type of psychopathology, the domain of creativity and the scales used to assess creativity.¹⁸

Considering the above, the purpose of the current study was to investigate the relationship between daydreaming, creativity and well-being and provide further evidence on the direction of this association. In addition, a late adolescent sample was used, as to the best of our knowledge, previous research on the subject matter has been primarily conducted on adults. Finally, a large sample size was collected ($n = 622$) and well-established scales with sound psychometric properties were used, so that reliable observations are made.

In total, five research hypotheses were proposed: H1) Daydreaming would be a statistically significant predictor of creativity; H2) Daydreaming would be a statistically significant predictor of overall distress (H2a), stress (H2b), anxiety (H2c) and depression (H2d); H3) There would be a statistically significant difference in daydreaming among severity levels of stress (H3a), anxiety (H3b) and depression (H3c); H4) Creativity would be a statistically significant predictor of overall distress (H4a), stress (H4b), anxiety (H4c) and depression (H4d); and H5) There would be a statistically significant difference in creativity among severity levels of stress (H5a), anxiety (H5b) and depression (H5c).

MATERIALS AND METHODS

Permissions and Participants

Prior to the distribution of the survey, approval was sought and received by a Scientific Review Committee (SRC). Data was collected online via Google Forms and

a sample of 622 Indian late adolescents (60.3% women), currently studying at Delhi University, was recruited. Participants had an age range between 18 to 21 years, with a mean age of 18.57 years ($SD = 0.67$). First, respondents were informed about the purpose of the study. Also, it was stated that their participation was voluntary and they could withdraw at any point in the study. Afterwards, participants were asked to provide their consent. Finally, respondents who agreed to participate in the study were presented with the questionnaire battery.

Survey Design and Testing

All respondents completed an online survey that consisted of 69 questions. The first two questions collected data about the age and gender of participants. The rest of the questions assessed respondents' daydreaming, creativity and well-being (Appendix A*).

Methodology and Data Collection

A questionnaire battery evaluating levels of daydreaming, creativity and distress was prepared. The scale examining distress comprised three subscales, stress, anxiety and depression. Sum scores were calculated for each scale and subscale, with higher scores indicating higher levels of the construct under investigation. Simple linear regression analyses were conducted for H1, H2 and H4, while one-way between-subjects ANOVAs were performed for H3 and H5.

In order to assess daydreaming in daily life, the Daydreaming Frequency Scale (DDFS) was used, which is one of the 28 scales included in the Imaginal Process Inventory.¹⁹ The DDFS contains 12 items ($\alpha = 0.90$), with responses provided on a 5-point Likert scale. Sample items are "I daydream instead of paying attention when I attend a meeting or a show that is not very interesting" and "I daydream whenever I have free time". Although response options differ among questions, in all items higher scores indicate a higher daydreaming frequency. Participants' everyday creativity was measured using the Biographical Inventory of Creative Behaviors (BICB).²⁰ The BICB includes 34 items ($\alpha = 0.88$) listing common creative activities and respondents indicate whether they engage in this activity (*yes*) or not (*no*). Sample items are "Organized an event, show, performance or activity" and "Invented and made a product that can be used". Finally, the Depression, Anxiety and Stress Scale - 21 Items (DASS-21)²¹ were used to examine distress. The DASS-21 consists of 21 questions ($\alpha = 0.91$) evaluating depression (7 items, $\alpha = 0.83$), anxiety (7 items, $\alpha = 0.76$) and stress (7 items, $\alpha = 0.78$) severity over the past week. Sample items are "I felt that I had nothing to look forward to", "I felt I

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was close to panic” and “I tended to over-react to situations”, respectively. Responses are provided on a 4-point Likert scale, ranging from 0 (*did not apply to me at all*) to 3 (*applied to me very much or most of the time*). Sum scores were computed for all scales and DASS-21 subscales, with higher scores indicating greater daydreaming, creativity, distress, depression, anxiety and depression. The data were analyzed using SPSS, version 25.0.

RESULTS

Results showed that greater daydreaming was related to lower well-being, but no association was identified with creativity. Also, higher creativity was related to higher anxiety and to lower depression severity. The rest of the findings were nonstatistically significant.

When H1 was analyzed, the results indicated a non-statistically significant model, $F(1,620) = 0.58$, $p = 0.45$, which accounted for less than 1% of the variance in creativity, ($R^2 = 0.001$; $R^2_{adj.} = -0.001$) (Table 1).

Table 1. Simple Linear Regression with Creativity as the Outcome Variable and Daydreaming as the Predictor Variable (N = 622)

Variable	B (95% CI)	SE _B	β	t	p
Daydreaming	-0.020 (-0.071, 0.031)	0.026	-0.030	-0.76	0.45

B = Unstandardized regression coefficient; CI = Confidence interval; SE_B = Standard error of unstandardized regression coefficient; β = Standardized regression coefficient.

Table 2. Simple Linear Regressions with Overall Distress, Stress, Anxiety and Depression as the Outcome Variables and Daydreaming as the Predictor Variable (N = 622)

Variable	B (95% CI)	SE _B	β	t	p
Overall distress	0.45 (0.36, 0.54)	0.045	0.38	10.07	<0.001
Stress	0.14 (0.11, 0.17)	0.015	0.35	9.33	<0.001
Anxiety	0.13 (0.10, 0.17)	0.016	0.32	8.26	<0.001
Depression	0.17 (0.14, 0.21)	0.018	0.35	9.33	<0.001

Proceeding with H2, results showed a statistically significant model for H2a [$F(1,620) = 101.38$, $p < 0.001$] that accounted for 13.9% of the variance in distress [$R^2 = 0.141$; $R^2_{adj.} = 0.139$], a statistically significant model for H2b [$F(1,620) = 86.97$, $p < 0.001$] that accounted for 12.2% of the variance in stress [$R^2 = 0.123$; $R^2_{adj.} = 0.122$] and a statistically significant model for H2c [$F(1,620) = 68.28$, $p < 0.001$] that accounted for 9.8% of the variance in anxiety [$R^2 = 0.099$; $R^2_{adj.} = 0.098$]. Also, a statistically significant model was identified for H2d [$F(1,620) = 87.04$, $p < 0.001$] that accounted for 12.2% of the variance in depression [$R^2 = 0.123$; $R^2_{adj.} = 0.122$]. Daydreaming was a statistically significant positive predictor of overall distress, stress, anxiety and depression, indicating that individuals who daydreamed more frequently were more likely to experience greater feelings of distress, stress, anxiety and depression (Table 2).

As to H3, the analysis suggested a statistically significant difference for H3a [$F(4,617) = 15.47$, $p < 0.001$, $\eta_p^2 = 0.091$], H3b [$F(4,617) = 12.80$, $p < 0.001$, $\eta_p^2 = 0.077$], and H3c [$F(4,617) = 19.99$, $p < 0.001$, $\eta_p^2 = 0.12$]. Bonferroni's post-hoc comparisons showed a significant difference in daydreaming between normal and mild stress ($p < 0.001$), normal and moderate stress ($p < 0.001$), normal and severe stress ($p < 0.001$), normal and extremely severe stress ($p < 0.001$) and mild and extremely severe stress ($p < 0.001$). Also, a significant difference in daydreaming between normal and mild anxiety ($p = 0.043$), normal and severe anxiety ($p = 0.003$), normal and extremely severe anxiety ($p < 0.001$), mild and extremely severe anxiety ($p = 0.018$), and moderate and extremely severe anxiety ($p < 0.001$) was identified. Finally, there was a significant difference in daydreaming between normal and mild depression ($p = 0.004$), normal and moderate depression ($p = 0.001$), normal and severe depression ($p < 0.001$), normal and extremely severe depression ($p < 0.001$), mild and extremely severe depression ($p < 0.001$), and moderate and extremely severe depression ($p < 0.001$). In all instances, individuals with higher stress, anxiety and depression severity displayed greater daydreaming (Table 3 and Figs. 1-3).

Table 3. Mean Differences in Daydreaming among Different Levels of Stress, Anxiety and Depression Severity

	Normal		Mild		Moderate		Severe		Extremely severe	
	M	SD	M	SD	M	SD	M	SD	M	SD
Stress	33.43	9.92	36.30	8.41	39.17	9.99	40.10	9.71	45.56	9.52
Anxiety	31.93	10.92	35.66	9.44	34.66	8.67	36.69	8.83	39.48	9.93
Depression	31.38	10.20	35.99	9.85	35.55	9.03	38.41	8.72	42.20	10.01

Concerning H4, the analysis indicated a nonstatistically significant model for H4a [$F(1,620) = 1.65$, $p = 0.20$] that accounted for less than 1% of the variance in distress [$R^2 = 0.003$; $R^2_{adj.} = 0.001$], as well as a nonstatistically significant model for H4b [$F(1,620) = 2.85$, $p = 0.092$] that accounted for less than 1% of the variance in stress [$R^2 = 0.005$; $R^2_{adj.} = 0.003$].

However, a statistically significant model was identified for H4c [$F(1,620) = 6.92$, $p = 0.009$] that accounted for 0.9% of the variance in anxiety [$R^2 = 0.011$; $R^2_{adj.} = 0.009$]. Creativity was a statistically significant positive predictor of anxiety, suggesting that respondents with greater creativity were more likely to experience higher anxiety.

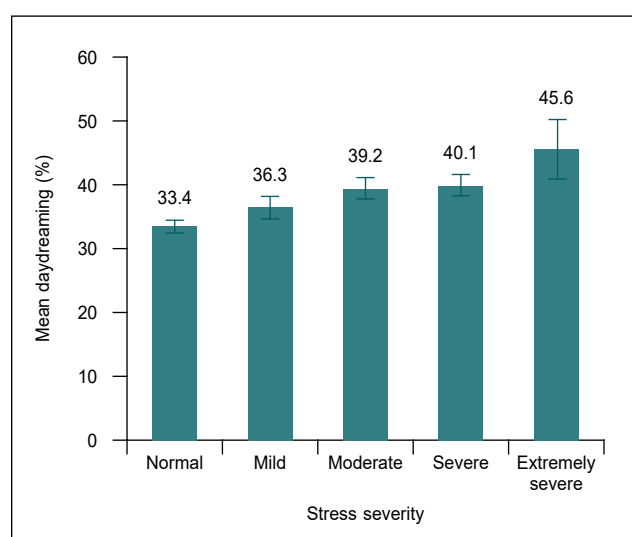


Figure 1. Mean differences in daydreaming among different levels of stress severity.

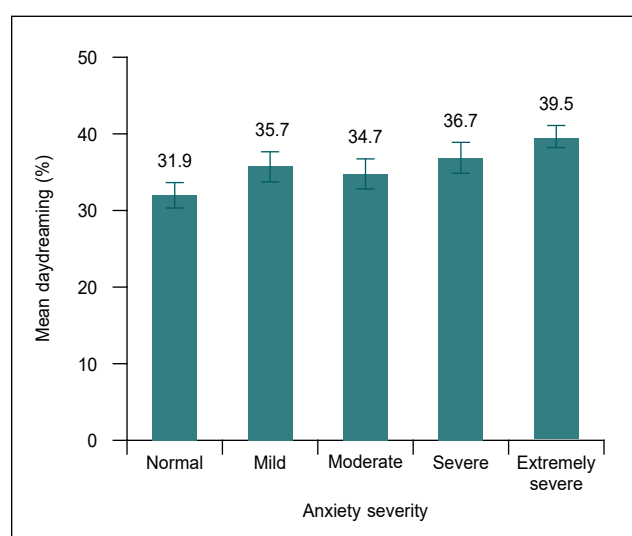


Figure 2. Mean differences in daydreaming among different levels of anxiety severity.

Finally, a nonstatistically significant model was identified for H4d [$F(1,620) = 0.31$, $p = 0.58$] that accounted for less than 1% of the variance in depression [$R^2 = 0.000$; $R^2_{adj.} = -0.001$] (Table 4).

Regarding H5, the analysis suggested a nonstatistically significant difference for H5a [$F(4,617) = 1.03$, $p = 0.39$, $\eta_p^2 = 0.007$]. However, a statistically significant difference was identified for H5b [$F(4,617) = 3.31$, $p = 0.011$, $\eta_p^2 = 0.021$] and H5c [$F(4,617) = 3.12$, $p = 0.015$, $\eta_p^2 = 0.020$].

Bonferroni's post-hoc comparisons showed a significant difference in creativity between normal and severe anxiety ($p = 0.018$) and between normal and extremely severe anxiety ($p = 0.025$).

Also, a significant difference in creativity between moderate and extremely severe depression was identified

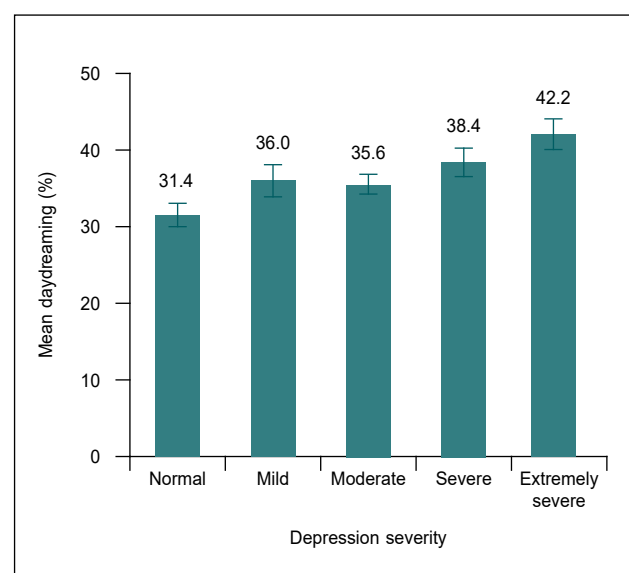


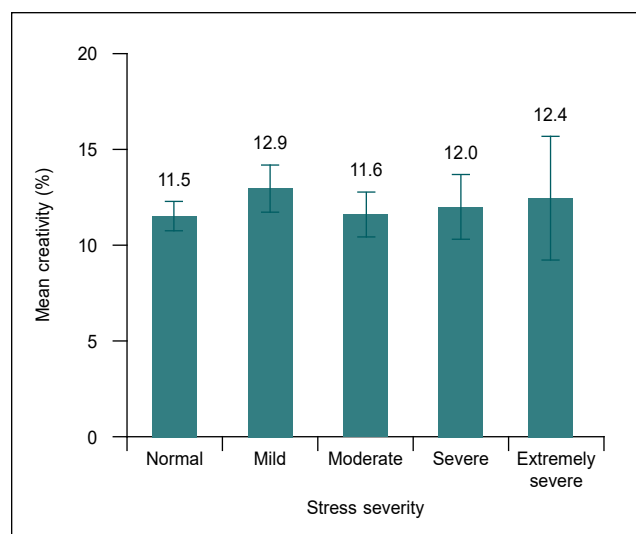
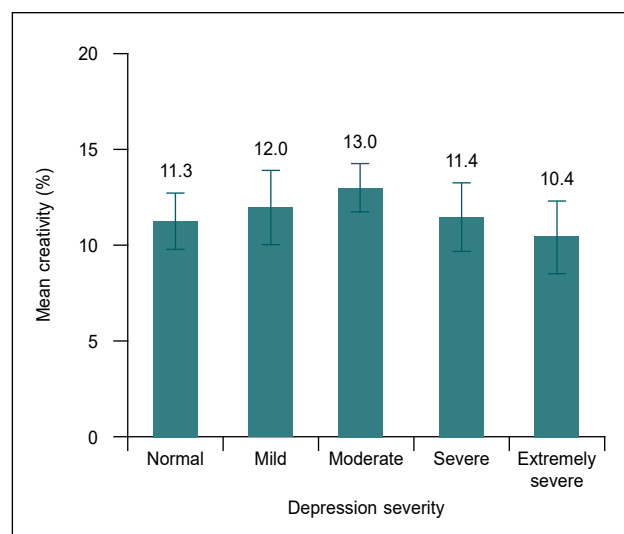
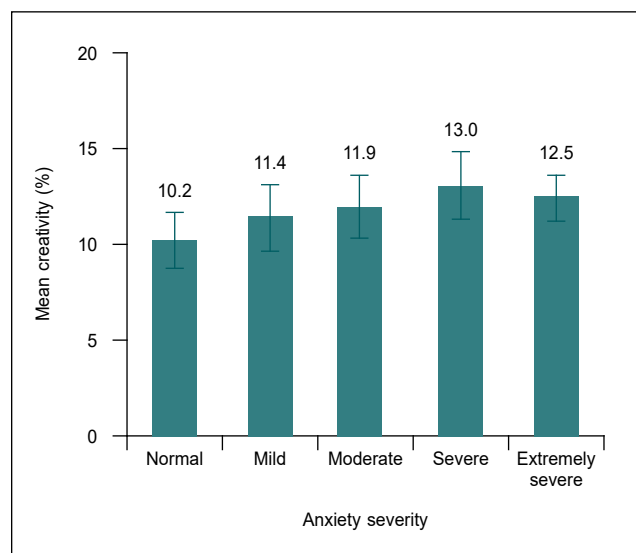
Figure 3. Mean differences in daydreaming among different levels of depression severity.

Table 4. Simple Linear Regressions with Overall Distress, Stress, Anxiety and Depression as the Outcome Variables and Creativity as the Predictor Variable (N = 622)

Variable	B (95% CI)	SE _B	β	t	p
Overall distress	0.095 (-0.050, 0.24)	0.074	0.052	1.29	0.20
Stress	0.043 (-0.007, 0.092)	0.025	0.068	1.69	0.092
Anxiety	0.069 (0.017, 0.12)	0.026	0.11	2.63	0.009
Depression	-0.017 (-0.076, 0.042)	0.030	-0.022	-0.56	0.58

Table 5. Mean Differences in Creativity among Different Levels of Stress, Anxiety and Depression Severity

	Normal		Mild		Moderate		Severe		Extremely severe	
	M	SD	M	SD	M	SD	M	SD	M	SD
Stress	11.46	6.59	12.87	6.47	11.58	6.53	11.98	6.38	12.38	6.63
Anxiety	10.25	5.61	11.41	5.92	11.91	7.00	13.00	7.37	12.46	6.60
Depression	11.27	5.78	11.95	6.48	13.01	7.26	11.38	6.35	10.41	5.96

**Figure 4.** Mean differences in creativity among different levels of stress severity.**Figure 6.** Mean differences in creativity among different levels of depression severity.**Figure 5.** Mean differences in creativity among different levels of anxiety severity.

($p = 0.017$). Individuals with higher anxiety severity reported greater creativity, whereas individuals with higher depression severity displayed lower creativity (Table 5 and Figs. 4-6).

DISCUSSION

Results showed that daydreaming was not a statistically significant predictor of creativity (H1). However, it was suggested that late adolescents who daydreamed more frequently were more likely to experience greater feelings of distress (H2a), stress (H2b), anxiety (H2c) and depression (H2d). Also, individuals with more severe stress (H3a), anxiety (H3b) and depression (H3c) engaged more frequently in daydreaming. Furthermore, late adolescents with higher creativity experienced greater anxiety (H4c). Nevertheless, creativity was not identified as a statistically significant predictor of distress (H4a), stress (H4b) and depression (H4d).

In addition, respondents with more severe anxiety reported higher levels of creativity (H5b), while a non-statistically significant difference among levels of stress severity was indicated (H5a).

Finally, it was interesting to observe that although depression did not predict creativity, participants with extremely severe depression displayed lower creativity than those with moderate depression (H5c).

The current study adopted a series of methodological steps to enhance the reliability of conclusions and contribute to the current body of knowledge. First, a large sample size was collected to increase the representativeness of observations. Also, scales with sound psychometric properties were used to accurately assess the constructs of interest. In addition, the analyses conducted allowed us to determine the predictive power of one variable on another, instead of solely evaluating the relationship among variables. Finally, the classification of distress subscales into severity levels revealed differences that would otherwise be shadowed if only sum scores were used.

However, certain limitations were also present. First, the sample comprised only Indian participants and the majority of them were female (60.3%). Hence, the lack of ethnicity and gender diversity might have influenced the results. Also, although well-established scales were used, these scales did not differentiate between types of daydreaming and creativity; a limitation that could have had an impact on the direction of the relationship among daydreaming, creativity and well-being. In addition, the analyses employed in this study do not allow causal inferences to be made. Finally, respondents may have been reluctant to provide honest responses in the items assessing distress and therefore, the possibility of social desirability bias cannot be excluded.

It is important that future research adopts advanced statistical techniques like Structural Equation Modeling (SEM) or experimental designs that would allow to determine if daydreaming and creativity lead to lower well-being or if individuals use daydreaming and creativity as a means to improve an already impaired well-being. In addition, scales that distinguish between types of daydreaming and creativity could be used and/or developed to identify potential differences. Moreover, qualitative research could provide in-depth insights on the experience of individuals and their perception of daydreaming and creativity benefits and drawbacks.

CONCLUSION

The objective of the current research was to explore the relationship among daydreaming, creativity, and well-being in late adolescents and a large sample of approximately 600 Indian individuals was recruited. Results showed that greater daydreaming was related to lower well-being, but no association was identified with creativity. Also, higher creativity was related to higher anxiety and to lower depression severity. Although these findings indicate a negative impact of daydreaming and

creativity on well-being, further research is required before practical implications are proposed. Therefore, it is aspired that this study will act as a source inspiration for scholars to advance knowledge in the subject matter and amend past and present methodological pitfalls.

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*APPENDIX A: Daydreaming, Creativity and Mental Well-Being

https://docs.google.com/forms/d/e/1FAIpQLSf-neo49C-hUWo0ZQMPNlJIB57EZrdUnXIK4qe9xDldhBFgsw/viewform?usp=sf_link

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Role of High-Quality Sleep in Tackling Chronic Stress, Depression and Anxiety

A recent study has highlighted the significance of high-quality sleep and effective coping strategies in preventing adverse mental health outcomes when faced with unpleasant or stressful experiences. The research, conducted during the protracted stressful period of the COVID-19 pandemic 2020, aimed to examine the impact of coping mechanisms on mental well-being and how sleep quality could enhance these effects. The study analyzed data from over 600 individuals participating in the Boston College Daily Sleep and Well-being Survey throughout the pandemic. In addition to sleep and mental well-being assessments, the surveys included baseline demographic information such as age, gender and ethnicity. The survey also gathered data on other factors, including alcohol consumption, quarantine status and physical activity levels. Dr Scott Cairney, the project's PhD Supervisor from the Department of Psychology at the University of York, explained the motivation behind the study and stated that while there is a positive association between high-quality sleep and overall health and well-being, they wanted to investigate whether this relationship would hold even in the face of intense and prolonged stress, as experienced by many during the pandemic. The study's findings showed the vital role of sleep in managing chronic stress and promoting well-being over an extended period. Quality sleep was found to be instrumental in reducing symptoms of depression and anxiety, thereby sustaining mental health. (Source: <https://www.mid-day.com/lifestyle/health-and-fitness/article/high-quality-sleep-key-to-manage-chronic-stress-reduce-symptoms-of-depression-and-anxiety-study-23297831>)

Government Launches Drive for 100% Coverage Under Ayushman Bharat PMJAY

The government of India has announced plans to initiate a large-scale enrollment drive for the Ayushman Bharat – Pradhan Mantri Jan Arogya Yojana (PMJAY) and has urged all states and Union Territories to register 100% of eligible individuals under the scheme. The announcement was made during the Swasthya Chintan Shivir, a 2-day conference organized by the Central Council of Health and Family Welfare. During the conference, Union Health Minister Mr Mansukh Mandaviya called upon the states and union territories to aim for universal coverage by involving health care workers at the grassroots level. The discussions at the conclave primarily focused on implementing the Ayushman Bharat PMJAY and the Ayushman Bharat Digital Mission. They addressed the gaps in coverage due to diverse local conditions and the level of digital health literacy across the country. Launched in 2018, Ayushman Bharat PMJAY aims to provide universal health coverage and free or affordable health care services to people residing in even the most remote areas. The scheme offers cashless medical services of up to Rs. 5 lakh per family per year, benefiting over 10.74 crore poor and vulnerable families, which accounts for more than 53 crore beneficiaries. According to government data, the Ayushman Bharat PMJAY has facilitated more than 4.34 crore hospital admissions, amounting to over Rs. 51,749.40 crore in authorized expenses. (Source: <https://health.economictimes.indiatimes.com/news/policy/govt-announces-drive-for-100-coverage-under-ayushman-bharat-pm-jay/101770542>)



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Laurence-Moon-Bardet-Biedl Syndrome: A Rare Case Report

MAHESH DAVE*, ANUJ GOYAL†, DEEPANSHU‡, RAM GOPAL SAINI‡, GAURAV DAVE#

ABSTRACT

Introduction: Laurence-Moon-Bardet-Biedl syndrome (LMBBS) is a rare autosomal-recessive disorder, which is characterized principally by cardinal symptoms of marked central obesity, retinal dystrophy, polydactyly, mental retardation, hypogonadism and renal dysfunction. **Case presentation:** We report a case of a 20-year-old male who presented to us with history of fever, vomiting and dizziness. He was incidentally diagnosed as a case of LMBBS as the patient was having polydactyly, retinitis pigmentosa, central obesity, hypogonadism and low IQ. **Conclusion:** Laurence-Moon-Bardet-Biedl syndrome is a very rare syndrome with very low incidence; hence, we are reporting this case. In addition, we advice more diligent approach from various specialties, so that this syndrome can be picked up at an early age.

Keywords: Laurence-Moon-Bardet-Biedl syndrome, polydactyly, hypogonadism

The Laurence-Moon-Bardet-Biedl syndrome (LMBBS) is a rare autosomal recessive disorder which is characterized by symptoms of obesity, polydactyly, retinitis pigmentosa, hypogonadism, mental retardation and renal dysfunction.¹ The frequency of the syndrome is estimated to be 1:1,60,000.² Less than 15 cases have been reported from India.³ LMBBS may also present with other secondary abnormalities, including speech disorder and developmental delay, ataxia, diabetes insipidus and dental crowding.⁴ Due to involvement of photoreceptors and macula in eyes, it leads to night blindness and pigmentary retinopathy finally leading to complete loss of vision in later part of disease.⁵ Truncal obesity with normal birth weight is present in archetypal patients.⁶ Postaxial polydactyly with extra digit in hand or toe is present. Further, hypogonadism may manifest either as small testes with micropenis in males or underdeveloped uterus and fallopian tubes with menstrual irregularities in females. Therefore,

LMBBS is a multiorgan involvement syndrome with rare occurrence and uneven life span.⁴ Hence, we hereby present a rare case of LMBBS.

CASE PRESENTATION

A 20-year-old male was patient admitted in medical ward, RNT Medical College, Udaipur, Rajasthan (India) with chief complaints of high-grade fever, vomiting and dizziness. On general physical examination, he was found to be overweight with central obesity. Incidentally, he was found to have 6 digits in all the four limbs (Fig. 1). On further enquiry, patient's mother gave a history of diminished vision from both the eyes since early childhood which was progressive in nature. They had consulted an ophthalmologist who diagnosed it as retinitis pigmentosa for which he was on symptomatic treatment without any improvement. Further, his parents gave history of mental retardation with low IQ and happy and cheerful behavior. On further evaluation, he was found to have micropenis with bilateral testicular atrophy with decreased secondary sexual characters. His height was 170 cm and weight 79 kg with a body mass index (BMI) of 27.33 (pre-obese).

After history and clinical examination, we put our diagnosis as acute febrile illness with retinitis pigmentosa, central obesity, polydactyly and hypogonadism clinically suspected to be LMBBS.

Patient was investigated extensively to confirm our clinical diagnosis. Complete hemogram revealed normal

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Figure 1. Showing hexadactyly in both lower limbs.



Figure 2. Fundus showing arterial attenuation, pale waxy disc with bony spicules in mid periphery.

hemoglobin levels, normal total leukocyte count, with mild thrombocytopenia ($10,000/\text{mm}^3$). Liver function tests showed normal bilirubin with mildly increased serum aminotransferase levels (SGOT 94 U/L and SGPT 80 U/L). Renal function tests were within normal limits. Urinalysis revealed proteinuria and glycosuria. Chest X-ray and ECG were normal. His fever profile revealed *Plasmodium falciparum* malaria. Ultrasonography showed mild hepatosplenomegaly with bilateral renal parenchymal Grade 1 disease with decreased testicular volume.

Specific investigations were done thereafter. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)

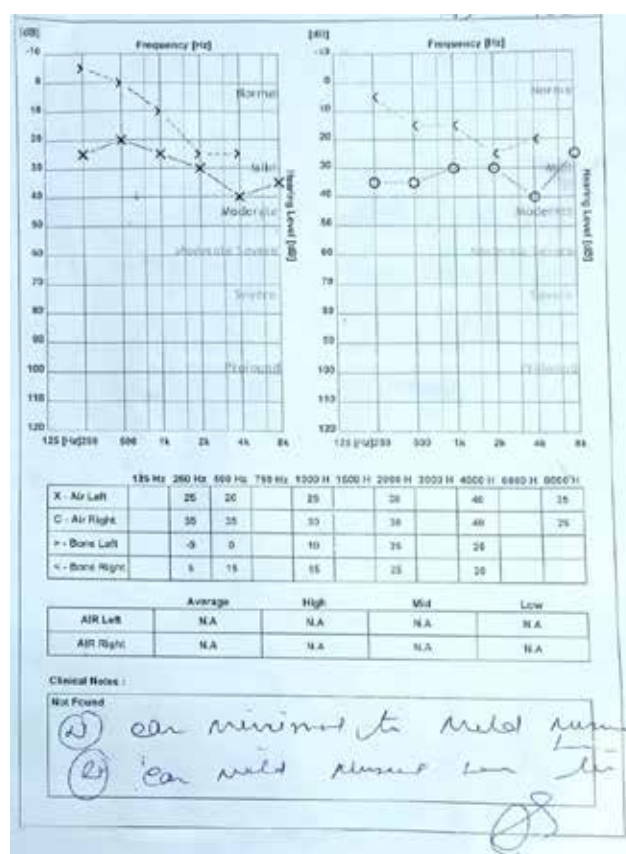


Figure 3. Pure-tone audiometry showing minimal to mild hearing loss in both the ears.

and testosterone levels were within normal limit but his prolactin levels were raised (400.6 uIU/mL). 2D-echocardiography was normal. Fundus examination revealed waxy pallor of disc, vessels attenuation and bony spicules in bilateral eyes (Fig. 2), which confirms the diagnosis of retinitis pigmentosa. Pure-tone audiometry revealed bilateral mild hearing loss (Fig. 3).

Hence, we confirm our diagnosis of LMBBS. The patient was treated symptomatically and discharged and was advised regular follow-up.

DISCUSSION

The LMBBS is an idiosyncratic, heterogeneous autosomal-recessive disorder with various clinical features requiring a multidisciplinary approach for early diagnosis. Literature has revealed that Laurence-Moon syndrome (LMS) and Bardet-Biedl syndrome (BBS) are two distinct disorders with overlapping features and very minute distinguishing elements between them.⁷ Most of the studies suggests that polydactyly and obesity is commonly observed in BBS, whereas spasticity is mainly seen in LMS but both of them can be considered same as LMBBS.⁸ So, we regarded our patient as LMBBS-a

Table 1. Modified Diagnostic Criteria for LMBBS Representing Primary Features

Primary features	Present (+) or absent (-)
Rod-cone dystrophy	+
Polydactyly	+
Obesity	+
Learning disabilities	+
Hypogonadism in males	+
Renal anomalies	+

globally acquired label to elucidate the illness.⁹ Apart from the cardinal manifestations, other features of the BBS include various degrees of intellectual impairment, congenital heart block, brachycephaly, deafness and dental anomalies. The full spectrum of clinical features is found in only 40% to 45% of LMBBS cases.¹⁰ The detailed biochemical mechanism that leads to BBS is still unclear. Twelve genes (BBS1 to BBS12) that are responsible for the disease have been cloned. The BBS proteins are components of the centrosome and affect the ciliary transport; hence, the disease falls under the spectrum of "ciliopathies".¹¹ In order to confirm the disease based on the clinical foundation, there is a revised criterion with certain primary/major features and secondary/minor features which are described in Tables 1 and 2.¹² For diagnosis of LMBBS, it requires 4 major or 3 major together with 2 minor traits to confirm the diagnosis as suggested by Forsythe and Beales.¹³ The chief complaint includes night blindness with photophobia and visual blurring.⁵ Truncal obesity, sometimes with diabetes mellitus is a prominent feature.⁵ Polydactyly is the most phenotypically evident abnormality with a prevalence of 69%.¹⁴ Hypogonadism is the final primary symptom with a prevalence of 59%, which may be diagnosed during the stage of puberty with delayed secondary sexual characteristics. This syndrome requires early diagnosis and a multidisciplinary approach for quality management. Treatment options are limited either to conservative therapy or surgical management as per the symptoms. Spectacles with visual aids can improve visual quality.¹⁵ Physical activity with low-calorie and high-protein diet can be helpful in obesity.¹⁶ Polydactyly can be treated surgically while testosterone supplementation can be given to combat hypogonadism. Further, regular follow-ups with endocrine monitoring should be done. Educational and behavioral assessment should be done by clinical psychologist. Family members counseling

Table 2. Modified Diagnostic Criteria for LMBBS Representing Secondary Features

Secondary features	Present (+) or absent (-)
Speech disorder/delay	+
Strabismus/cataract/astigmatism	+
Brachydactyly/syndactyly	+
Developmental delay	+
Polyuria/polydipsia	-
Ataxia/poor coordination/imbalance	-
Mild spasticity	-
Diabetes mellitus	-
Dental crowding/hypodontia/small roots/high arched palate	-
Left ventricular hypertrophy/ Congenital heart diseases	-
Hepatic fibrosis	-

sessions to be done for better patient care. Community needs to welcome these patients and not treat these patients with hatred and inequity. This can help in upgrading their status of living.

CONCLUSION

Laurence-Moon-Bardet-Biedl syndrome is rare entity with very low incidence. Even though the patient was seen by different specialists earlier, the diagnosis was missed due to the rarity of this condition. This case report highlights the features required to diagnose this syndrome and will help in diagnosis of this syndrome at an early age.

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Intensive Exercise Shows Potential for Slowing Parkinson's Disease Progression

A study titled "Intensive exercise ameliorates motor and cognitive symptoms in experimental Parkinson's disease by restoring striatal synaptic plasticity," published in the journal *Science Advances*, showed that intensive exercise could potentially slow the progression of Parkinson's disease.

The research was conducted by neuroscientists from the Faculty of Medicine of the Catholic University, Rome Campus, and the A Gemelli IRCCS Polyclinic Foundation, in collaboration with various institutes, including the San Raffaele Telematic University Rome, CNR, TIGEM, University of Milan, and IRCCS San Raffaele, Rome, to unveil a novel mechanism that explains the positive effects of exercise on brain plasticity.

Previous research has shown a correlation between intensive physical activity and increased production of a critical growth factor called brain-derived neurotrophic factor (BDNF).

The findings of the study showed that daily treadmill training sessions led to a reduction in the spread of pathological alpha-synuclein aggregates. These aggregates are responsible for neurons' gradual and progressive dysfunction in specific brain areas crucial for motor control, known as the nigrostriatal pathway.

The study showed that the neuroprotective effect of physical activity was also associated with the survival of dopamine-releasing neurons and the ability of striatal neurons to express a form of dopamine-dependent plasticity, which is impaired by Parkinson's disease.

Furthermore, the researchers discovered that BDNF, whose levels increase with exercise, interacts with the NMDA (N-methyl-D-aspartate) receptor for glutamate. This interaction enables neurons in the striatum to respond effectively to stimuli, leading to effects that persist beyond the duration of the exercise practice. (Source: <https://medicalxpress.com/news/2023-07-parkinson-disease-intense-bay.html>)

Vitamin D Deficiency Eradication: A National Priority

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NUTRITION AND HEALTH

Nutrition is a major determinant of health. Food security and caloric sufficiency have contributed, in no small measure, to the improvement in lifespan and overall health observed across most of the globe.

Various facets of nutrition, apart from protein and energy balance, have been explored and addressed by researchers. One example is iodine nutrition. A well-known micronutrient, its fortification of salt has led to near-universal eradication of iodine deficiency disorders (IDD) and their resultant complications. Severe cases of cretinism and goiter are now a medical rarity. Credit for this achievement goes to clinical science and community medicine: to clinical endocrinology for understanding the link between iodine, thyroid function and physical/mental health, and to public health, for translating this knowledge to awareness, advocacy and action; the action being iodine supplementation.

MALNUTRITION AND HIDDEN HUNGER

Malnutrition, however, remains a major challenge even in today's world. India is the biggest contributor of undernourished people in the world, with around

194.4 million people, or 14.37% of its population, not receiving enough nutrition. India has one of the worst rates of child malnutrition in the world, with one-third of malnourished children globally being Indian.¹ Advances in science and medicine have uncovered unique forms of malnutrition, termed 'hidden hunger' (Table 1). These include deficiencies in micronutrients such as vitamins, minerals and electrolytes. Suboptimal intake of these nutrients can lead to a wide spectrum of disorders and diseases. Individual ill health influences the health of the family and of the society and nation as well.²

Micronutrient malnutrition is a public health problem in several developing nations. Micronutrient malnutrition is a huge economic problem as well. The short-term economic cost of micronutrient malnutrition in India amounts to 0.8% to 2.5% of the gross domestic product.²

VITAMIN D AND HEALTH

In this regard, one important micronutrient is vitamin D. Studies from India have reported a wide range of vitamin D deficiencies, from 30% to as high as 100%. Community-based studies conducted in the last 10 years have shown a prevalence range of 50% to 94% of vitamin D deficiency in India.^{3,4}

This moiety is actually a hormone with multiple effects, including musculoskeletal, metabolic, mitogenic and anti-miasmic (related to immunity). Epidemiological studies have revealed the high prevalence of vitamin D deficiency across all geographical areas of India in all population subsets. Research also documents the results of such deficiency on the musculoskeletal system and other organ systems. The health economic impact of hidden hunger is significant.

Table 1. The Spectrum of Hidden Hunger

Micronutrient deficiency
• Minerals – Ca, Fe, I
• Vitamins – D, B complex, A
• Electrolytes/fluids – Na, K, water

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The relevance of the widespread deficiency and necessity for supplementation has been debated. While vitamin D may not be a panacea, its strong association with chronic diseases and acute conditions has been highlighted. Hence, it is an important, inexpensive and safe therapy for several diseases and in different phases of life, such as pregnancy, childhood and old age.⁵

VITAMIN D SUPPLEMENTATION

Due to its diverse and multidimensional impacts on the overall health of individuals, vitamin D is an important contributor to national health. As clinicians and community medicine experts, it is time to start a nationwide campaign to eradicate vitamin D deficiency. Just as previous campaigns against IDD, and current efforts against iron deficiency anemia, this fight for vitamin D sufficiency will have significant public health benefits. We have already witnessed the success of the IDD Control Program in India, with sustained political commitment, the increased production of iodized salt, and involvement of the private sector, the institution of legislation to ensure the iodization of salt, and the catalytic role played by academic institutes, civil society and international agencies.⁶ Adopting the best practices from such successful programs and current situational analysis, a vitamin D deficiency eradication policy plan needs to be devised and implemented. Vitamin D sufficiency will be associated with better musculoskeletal competency, functionality and quality of life. Along with savings accrued by minimizing work hours lost in seeking health care, vitamin D sufficiency will enhance productivity and economic health.

METHODS OF VITAMIN D SUPPLEMENTATION

Vitamin D is available through sunlight and food. However, the duration and extent of sun exposure required are difficult to achieve for most individuals. Though food fortification has been suggested as a means of improving vitamin D status, it is difficult to achieve adequate levels through this method. Fortification of milk is also not allowed in India, as it amounts to 'adulteration', coupled with the fact that vitamin D is hardly present in vegetarian, especially vegan, diets, vitamin D supplementation is required for most persons. While those with symptomatic/or documented

deficiency require higher doses for replacement, supposedly 'asymptomatic', individuals may also benefit from supplementation with doses mentioned in the recommended daily allowance. As the National Institute of Nutrition (NIN) recommends 600 IU/day,⁷ a monthly dose of 60,000 IU should be deemed practical and prudent. Vitamin D supplementation may be integrated into existing national health care programs.

Relevant caveats, of course, must be kept in mind while suggesting vitamin D supplementation as a public health measure. Overdosage should be avoided, and persons with comorbid diseases like endocrine, renal or hepatic disease must be referred to appropriate specialists. National health is everyone's right and everyone's responsibility. Enhancing awareness about the importance of vitamin D sufficiency is the first step towards achieving this goal.

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Principles of Ethics in Medical Research

The 12 general principles of ethics in medical research as described in the “Indian Council of Medical Research. Ethical Guidelines for Biomedical Research on Human Subjects 2006” guidelines are as below. These are common to all areas of biomedical research.

1. **Principles of essentiality:** Whether the research is considered to be absolutely essential after a due consideration of the existing knowledge in the proposed area of research. The proposed research should be carefully examined by an independent and responsible body of persons who, after careful consideration, come to the conclusion that the said research is necessary for the advancement of knowledge and for the benefit of mankind and environment.
2. **Principles of voluntariness, informed consent and community agreement:** The participants are to be informed about the research and the impact and risk of the research on them and others. They should be informed about their right to abstain from further participation in the research irrespective of any legal or other obligation that either they may have been entered into or by someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding.
3. **Principles of non-exploitation:** All research participants are remunerated for their involvement in the research or experiment. They should be kept fully apprised of all the dangers arising in and out of the research, irrespective of their social and economic condition or status, or literacy or educational levels, so that they can understand all the physical and psychological risks including the moral implications of the research whether to themselves or others, including future generations.

Each research shall include an in-built mechanism for compensation for the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, including treatment during and after the research or experiment.
4. **Principles of privacy and confidentiality:** The identity and records of the human participants of the

research or experiment are to be kept confidential as far as possible. No details about the identity of human participants are to be disclosed without valid scientific and legal reasons without the specific consent, in writing, of either the human participant concerned, or someone authorized on their behalf. It should be ensured that the participant has come to no harm, or does not face any discrimination or stigmatization as a consequence of having participated in the research or experiment.

5. **Principles of precaution and risk minimization:** All precautions should be taken at all stages of the research so that the study participant and those affected by it including the community are put to the minimum risk, suffer from no known irreversible adverse effects and generally, benefit from the research or experiment.
6. **Principles of professional competence:** The research is conducted at all times by competent and qualified persons who act with total integrity and impartiality. They should be aware of, and are mindful of, preferably through training, the ethical considerations to be borne in mind in respect of such research or experiment.
7. **Principles of accountability and transparency:** The research is to be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research. Any conflict of interest should be disclosed. All records pertaining to the research including data and notes should be retained for the prescribed time period or as required by the law, or for conducting further research such as post research monitoring.
8. **Principles of the maximization of the public interest and of distributive justice:** The research and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged; and in particular, the research participants themselves and or the community from which they are drawn.
9. **Principles of institutional arrangements:** All persons connected with the research have the duty to ensure that all the required procedures are

complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in a bonafide and transparent manner. All research reports, materials and data connected with the research are to be duly preserved and archived.

10. **Principles of public domain:** The findings of the research should be brought into the public domain so that its results are generally made known through scientific and other publications subject to such rights as are available to the researcher and those associated with the research under the law in force at that time.
11. **Principles of totality of responsibility:** All those directly or indirectly connected with the research or experiment including the researchers, those responsible for funding or contributing to research funding, the institution/s or where the research

is conducted and the various persons, groups or undertakings who sponsor, use or derive benefit from the research, market the product (if any) or prescribe its use are entrusted with the professional and moral responsibility, for the due observance of all the principles, guidelines or prescriptions laid down generally or in respect of the research or experiment in question.

12. **Principles of compliance:** There is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human participant to ensure that both the letter and the spirit of these guidelines, as well as any other norms, directions and guidelines which have been specifically laid down or prescribed and which are applicable for that area of research or experimentation, are scrupulously observed and duly complied with.



Neighborhood Characteristics Independently Impact COVID-19 Hospitalizations: Study

A study published in *PLoS ONE* suggested that the built environment of neighborhoods plays an independent role in determining the risk of individuals being hospitalized due to coronavirus disease 2019 (COVID-19).

The study examined neighborhood characteristics in the Denver Metro Area and their association with hospitalizations among 18,042 people who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between May and December 2020, before the widespread availability of vaccines.

The study findings showed that neighborhoods with higher public transit quality and accessibility were associated with a higher incidence rate of hospitalization. The study also identified differences between the two largest ethnic groups in the region. Latinx individuals had a higher hospitalization rate in areas with higher PM2.5 levels, while density and overcrowding showed stronger associations for non-Hispanic White individuals.

After accounting for biological factors, the study identified four neighborhood characteristics that contributed to COVID-19 hospitalizations, namely density and overcrowding, environmental hazards (such as air pollution and proximity to highways), environmental amenities (including access to parks), and mobility options (such as public transit, walkability and bike-ability).

The authors were not surprised by the finding that individuals with compromised lung and immune systems exposed to chronic air pollution would have a higher risk of severe disease and hospitalization after contracting COVID-19.

Furthermore, the study highlighted the disproportionate impact of air pollution on People of Color, as higher PM2.5 levels affected Latinx individuals more than non-Hispanic White individuals. (Source: <https://www.news-medical.net/news/20230714/Neighborhood-environment-can-increase-risk-of-COVID-19-hospitalization-study-reveals.aspx>)

India Live 2023

FFR-OCT IN LEFT MAIN

Dr DS Chadha, Bengaluru

The angiographic evaluation of left main (LM) disease can present challenges and requires use of additional devices (intravascular imaging/coronary physiology) to make the correct decision regarding revascularization. There is a lot of anatomical and functional mismatch in the LM implying that even 40% to 50% stenosis can be functionally significant.

Fractional flow reserve (FFR) evaluation of the LM depends not only on the lesion characteristics but also on the territory supplied by the vessel. FFR is very reliable in the presence of isolated LM disease. It is accepted that an FFR in the LM <0.8 or an minimum luminal area (MLA) $<6 \text{ mm}^2$ is the threshold for revascularization. FFR is a potential tool for assessing the hemodynamic significance of an LM stenosis.

A poor correlation has been noted between quantitative coronary angiography and FFR, which points to the shortcomings of relying on angiography alone in evaluating LM lesions. Angiographically intermediate LM lesions with an FFR of ≥ 0.80 can have revascularization deferred with favorable long-term outcomes.

Optical coherence tomography (OCT) provides precise information very quickly and helps treat cardiovascular diseases, including LMCA disease. OCT can help assess atherosclerotic plaque and visualize thrombus. It can also assist in evaluating the lumen area with accurate automated measurements. OCT is indispensable in patients where the LM disease is present along with disease in left anterior descending (LAD) and left circumflex artery (LCx).

During percutaneous coronary intervention (PCI), it can help in assessing lesion morphology and measuring the diameter and plaque burden in both LCx and LAD. It formulates the stenting strategy and will guide whether the lesion can be treated with single-stent or two-stent strategy. Post-stenting the OCT helps in optimizing the

stent as there is a lot size mismatch between the LM and its daughter vessels.

There is a benefit in integrating FFR and OCT technologies for evaluating coronary artery disease (CAD). FFR helps identify significant lesions which can then be precisely treated with coronary stents using OCT. OCT-guided stenting is associated with good long-term results and very low rates of stent failure. This is most important in the LM segment as it supplies a big chunk of myocardium and stent failure in this segment can be catastrophic.

HOW WILL WE APPROACH CORONARY ARTERY DISEASE IN 2033?

Dr Patrick W Serruys, Ireland

In a lifespan, we will see a tremendous evolution of lipid-lowering and anti-inflammatory therapies. Nowadays, CAD phenotype on noninvasive imaging is a sufficient argument to initiate primary preventive pharmacotherapy.

PCSK9 is an endogenous regulator of low-density lipoprotein (LDL) receptor levels by facilitating the destruction of the LDL receptor. Inclisiran is a small interfering or silencing RNA, silencing the gene that encodes mRNA responsible for the production of PCSK9, with a consequence of an increase in activity in LDL receptor, now recycled, thereby lowering your LDL cholesterol to a very low level. CT is a safe alternative to cardiac catheterization for patients with suspected CAD that will likely change clinical practice worldwide by replacing invasive testing in patients with stable chest pain with an intermediate pretest probability for obstructive disease. The value of multislice CT as a diagnostic “one-stop shop” (coronary CT angiogram, finite element analysis, computational fluid dynamics, tissue characterization analysis, perivascular fat attenuation analysis, wall shear stress and wall strain, etc.) is currently emerging as the most promising, cost-effective and best-reimbursed approach to identify coronary disease throughout the lifespan.

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News and Views

A New Treatment for Alzheimer's Disease Gets Full FDA Approval

Lecanemab-irmb, an amyloid beta-directed antibody, marketed by the name of Leqembi, has been granted full approval by the US Food and Drug Administration (FDA) for adult patients with Alzheimer's disease. It is the first such treatment for the treatment of Alzheimer's disease and is administered as an IV infusion once every 2 weeks. Leqembi, which received accelerated approval in January this year, acts by reducing the amyloid plaques in the brain, the hallmark of Alzheimer's disease.

Indication: Patients with mild cognitive impairment or mild dementia stage of Alzheimer's disease.

Contraindication: Hypersensitivity to lecanemab-irmb or to any of its inactive ingredients. The drug should be avoided in advanced stage of the disease.

Adverse effects: Angioedema, anaphylaxis, headache, infusion-related reactions.

Warning and precautions:

- Amyloid-related imaging abnormalities (ARIA) - temporary swelling in brain areas - can occur; symptoms, if they occur, include headache, confusion, dizziness, vision changes and nausea. Rarely, life-threatening brain edema or intracerebral hemorrhages can occur.
- Patients should be closely monitored via brain imaging.
- Patients should be investigated for ApoE ε4 before initiating treatment as patients who are homozygous for the ApoE ε4 allele are at greater risk of developing serious and severe ARIA.
- Exercise caution when using this drug in patients on anticoagulants or other risk factors for intracerebral hemorrhage.

(Source: FDA News Release: FDA converts Novel Alzheimer's disease treatment to traditional approval. July 06, 2023. <https://www.fda.gov/news-events/press-announcements/fda-converts-novel-alzheimers-disease-treatment-traditional-approval>. Accessed July 8, 2023.)

Prompt Treatment of Endometriosis Improves Quality of Life

Endometriosis has a significant impact on the quality of life for the affected women. To examine the

interrelationship between health-related quality of life (HRQoL) and endometriosis, researchers from The University of Queensland examined 3,728 women using data from the Australian Longitudinal Study on Women's Health.¹

The 36-item Short Form Survey (SF-36) was utilized to assess the HRQoL every 3 years over a period of 22 years from 1996 to 2018. SF-36 covers eight domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotion and mental health function. Women who scored below the 25th percentile had lower HRQoL and those who score above the 25th percentile had higher HRQoL. Endometriosis was classified as clinically suspected endometriosis (self-reported) or surgically confirmed endometriosis.

Analysis of data over the eight surveys revealed a poorer HRQoL in women with endometriosis during the course of the study with worse scores on all the eight domains of SF-36. The odds ratio (OR) for worse scores on all the eight domains were found to be 1.33 for physical functioning, 1.57 for role physical, 1.65 for bodily pain, 1.61 for general health, 1.38 for vitality, 1.38 for social functioning, 1.19 for role emotion and 1.32 for mental health. "Women with endometriosis also had significantly lower physical health 1.68 and mental health components scores 1.28" noted the authors.

This study highlights the impact of endometriosis on mental, physical and social well-being and function of the women with endometriosis compared to those without endometriosis. The strongest association was observed between endometriosis and bodily pain. Next came general health and role physical. Endometriosis-related pain and associated anxiety, stress and depression have been hypothesized to be the underlying reason for the association between endometriosis and HRQoL.

"Our findings highlight the importance of early diagnosis of endometriosis and managing the patients promptly with pain and psychological treatment to boost their quality of life" concluded the authors.

Reference

1. Gete DG, et al. Impact of endometriosis on women's health-related quality of life: a national prospective cohort study. *Maturitas*. 2023;174:1-7.

Both Optimal Sleep and Higher Physical Activity Vital for Better Cognitive Health

Poor sleep may offset the protective effects of physical activity on cognition in older adults, according to a new study from the University College London, UK published in the journal *Lancet Healthy Longevity*.

To investigate the impact of sleep and physical activity on cognition, researchers examined data of 8,958 participants, aged 50 to 95 years. From the English Longitudinal Study of Ageing collected from January 2008 through July 2019. Episodic memory was assessed every 2 years, for a median follow-up of 10 years, via immediate and delayed recall tasks and verbal fluency with an animal naming task. None of the participants had any cognitive impairment at the time of recruitment. Based on both frequency and intensity of activity, physical activity was categorized as lower or higher physical activity; sleep duration was categorized as short (<6 hours), optimal (6-8 hours) or long (>8 hours). People with self-reported dementia and who were found to have some cognitive impairment were excluded from the study.

At baseline, participants who were less physically active and those with suboptimal sleep performed poorly on cognitive tests. Those who were more physically active and had optimal sleep scored higher on cognitive assessment versus combinations of lower physical activity and sleep categories. The baseline cognitive performances among participants with higher physical activity in the various sleep categories were comparable. After 10 years, decline in cognition was rapid even among participants in the higher physical activity group who slept for less than 6 hours compared to those who slept for 6 to 8 hours. Their cognitive scores were similar to those who were less physically active. When data was analyzed based on sex, long sleep was associated with a more favorable cognitive trajectory among men only. The cognitive benefits of combination of higher physical activity and long sleep were more evident in men. In this study, both optimal sleep and higher physical activity had an independent association with better cognitive function, whereas short sleep was associated with faster cognitive decline regardless of physical activity. Based on their findings, researchers concluded that “physical activity interventions should also consider sleep habits, to maximize benefits of physical activity for long-term cognitive health”.

Reference

1. Bloomberg M, et al. Joint associations of physical activity and sleep duration with cognitive ageing: longitudinal analysis of an English cohort study. *Lancet Healthy Longev*. 2023;4(7):e345-53.

Factors Predicting Uncontrolled Asthma

Thirty percent of patients with type 2 (T2)-high or uncontrolled asthma have higher blood eosinophil counts, serum IgE and fractional exhaled nitric oxide (FeNO) levels, suggests a study published in the *Annals of Allergy, Asthma & Immunology*.¹

This study recruited 133 patients with type 2 asthma, aged ≥18 years; 23 patients had blood eosinophil counts (BECs) ≥300 cells/μL, serum-free IgE ≥120 ng/mL and their FeNO ≥25 parts per billion (ppb). These patients were categorized as Group 1. Eight-seven patients with higher levels of one or two of the biomarkers were put into Group 2, while in Group 3, 23 patients had lower values of all the three biomarkers. The objective of the study was to define optimal cut-off values of markers of T2 inflammation that were predictive of uncontrolled asthma.

Results showed significantly higher levels of sputum eosinophils, blood eosinophil-derived neurotoxin (measured by enzyme-linked immunosorbent assay [ELISA]) and Siglec8+ eosinophils (measured by flow cytometry) but lower forced expiratory volume in 1 second (FEV1) in Group 1 patients. The prevalence of poorly controlled asthma was also higher in this group; 30.4% had uncontrolled asthma, 43.5% had partly controlled asthma, while 26.1% had well-controlled asthma. In Group 2, asthma was well-controlled in 54% and less than 10% had uncontrolled asthma. None of the patients in Group 3 had uncontrolled asthma and 30% having partly controlled asthma. The increase in FeNO levels (54.3 vs. 28.8 in well-controlled asthma) and BECs (786.7 μL vs. 279.1 μL in well-controlled asthma) in patients with uncontrolled asthma was statistically significant. Although nonsignificant, serum IgE levels were higher in uncontrolled asthma (488.2 ng/mL vs. 298.2 ng/mL).

The optimal cut-off values for predicting uncontrolled asthma were found to be FeNO levels of 22 parts per billion, blood eosinophil counts 161.4 cells/L and serum-free IgE levels of 85.9 ng/mL.

Therefore, the determination of cut-off values of the three T2 biomarkers can help to identify patients who need treatment with additional T2 biologics, despite being on maintenance asthma treatment including inhaled corticosteroids.

Reference

1. Woo SD, et al. Biomarkers for predicting type 2-high and uncontrolled asthma in real-world practice. *Ann Allergy Asthma Immunol*. 2023;S1081-1206(23)00339-3.

Chronic Pain Disorder Associated with Increased Risk of Premature Death

A recent study published in the open-access journal *RMD Open* has shed light on the potentially increased vulnerability of individuals living with fibromyalgia, a chronic pain disorder characterized by widespread pain and fatigue, to early mortality.

The study, conducted by researchers from the Ben-Gurion University of the Negev in Israel, suggested that fibromyalgia may amplify painful sensations by affecting the processing of pain signals in the brain and spinal cord.

To support their hypothesis, the researchers examined the results of 6 relevant studies published between 1999 and 2020 involving a total of 1,88,751 adults who had other co-existing health conditions.

The analysis revealed that individuals with fibromyalgia faced a 27% higher risk of death from all causes than the general population.

The study also showed that the risk of death from cancer was 12% lower among individuals with fibromyalgia than those without the condition. The risk of accident death was only marginally higher (5%).

However, the risk of death from infections, including pneumonia and septicemia, was 44% higher for individuals with fibromyalgia. Furthermore, the risk of death by suicide was more than 3 times higher than the general population. (Source: <https://www.daijiworld.com/news/newsDisplay?newsID=1098732>)

New Study Establishes a Link Between Gum Disorder and Alzheimer's Disease

According to a study published in the *Journal of Neuro-inflammation*, researchers have found a link between periodontal disease and the formation of amyloid plaque, a hallmark of Alzheimer's disease.

The study conducted by researchers from the Forsyth Institute in the US revealed a connection between gum disease and changes in brain cells known as microglial cells. They explained that these cells are crucial in defending the brain against amyloid plaque.

The study focused on microglial cells, a specific type of white blood cell responsible for breaking down amyloid

plaque. They discovered that when these cells were exposed to oral bacteria, they became overactive and consumed excessive amounts of amyloid plaque.

This finding had a significant implication as it demonstrated the impact of gum disease on overall health.

Gum disease can lead to lesions between the gums and teeth, allowing bacteria to pass through the blood-brain barrier—a protective layer that lines the inner surfaces of blood vessels in the brain—and trigger a response from microglial cells in the organ.

To further investigate this connection, the researchers isolated microglial cells from the brain and exposed them to oral bacteria. This exposure resulted in the overstimulation of microglial cells, leading to neuro-inflammation and alteration in the interaction of microglial cells with amyloid plaques. (Source: <https://www.tribuneindia.com/news/health/new-study-links-gum-disorder-to-alzheimers-disease-524805>)

Triple Combination Therapy Enhances Cystic Fibrosis Treatment

A study published in the *European Respiratory Journal* showed that triple combination treatment could produce long-term benefits, such as reduced lung inflammation and the stickiness of mucus in the airways in individuals with cystic fibrosis.

The study led by Prof Marcus Mall and his team, building upon a previous Charite-led study, has investigated the long-term benefits of triple drug combination therapy for patients with cystic fibrosis. The therapy consisted of elexacaftor, tezacaftor and ivacaftor. The therapy was observed to improve lung function and quality of life. The researchers aimed to determine if these positive effects persisted over 12 months or longer. To assess the long-term impact, they analyzed sputum samples collected from the respiratory tracts of 79 adolescents and adults with cystic fibrosis and chronic lung disease. The findings of the study demonstrated that combination therapy led to a reduction in the viscosity of respiratory secretions. Additionally, the treatment resulted in a decrease in lung inflammation and bacterial infections among the patients. (Source: <https://www.hindustantimes.com/lifestyle/health/how-triple-combination-therapy-improves-cystic-fibrosis-study-101689050492826.html>)

■ ■ ■ ■

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Why Do We Apply Holy Ash?

Bhasma is the holy ash produced from the Homa, the sacrificial fire, wherein special wood along with ghee and other herbs are offered as a part of pooja. By the time Bhasma is formed, no trace of original matter remains in the ash. Ash obtained from any burnt object is not Bhasma. The ritual involves worshipping the deity by pouring ash as Abhishek and then distributing it as Bhasma, which is then applied on the forehead (usually), upper arms, chest or rubbed all over the body. Some consume a pinch of Bhasma when they receive it. The word Bhasma is derived from “bha” or “bhartsanam” (“to destroy”) and “sma” or “smaranam” (“to remember”). It denotes “that by which our sins are destroyed and the Lord is remembered”. Bhasma is also called Vibhuti, which means glory. Bhasma is associated with Lord Shiva who applies it all over His body.

Spiritually, the Homa is the offering of oblations into the fire with sacred chants and signifies offering or surrender of the ego and egocentric desires into the fire

of knowledge. The resultant ash signifies the purity of the mind. The fire of knowledge burns the oblation and wood signifying ignorance and inertia, respectively. The application of ash implies that one should burn false identification with the body.

Bhasma has medicinal values in Ayurveda. It is supposed to be the strongest of all Ayurveda preparations. According to Ayurveda, a Bhasma is formed when the matter is converted into non-matter by the process of Homa. The non-matter is the spirit or the energy of the matter being processed with strong healing powers. It has the same significance as any ‘potentized’ medicine in Homoeopathy. It absorbs excess moisture from the body and prevents colds and headaches.

When applied with a red spot at the center, the mark symbolizes Shiva-Shakti (the unity of energy and matter that creates the entire seen and unseen universe). The Upanishads say that the famous Mrityunjaya Mantra should be chanted whilst applying ash on the forehead.

■ ■ ■ ■

Right Ventricular Diastolic Diameter: A Prognostic Indicator in COPD Patients

Cardiovascular diseases are one of the most frequent comorbid conditions in patients with chronic obstructive pulmonary disease (COPD). Management of COPD therefore should also include evaluation of comorbidities and their appropriate treatment. Echocardiography serves as a useful tool to evaluate the heart in these patients.

COPD patients with right ventricle diastolic diameter >38 mm are more likely to have unfavorable prognosis, according to a study presented at ATS 2023, the international conference of the American Thoracic Society. The study findings were also published in the *American Journal of Respiratory and Critical Care Medicine*.¹

This study enrolled 35 patients with COPD with preserved left ventricular ejection fraction (LVEF), who underwent spirometry and transthoracic echocardiogram (TTE) along with clinical examination as part of the study protocol. The objective of the study was to identify factors on echocardiography that were predictive of adverse outcomes characterized as hospitalization due to any cause, nonfatal cardiac events and mortality. The study duration was for 1 year. During the course of the study, adverse outcomes occurred in 10 patients and were seen as COPD with higher right ventricular diastolic diameter or lower LVEF or lower functional vital capacity. COPD patients with right ventricular diastolic diameter higher than 38 mm presented with an area under the ROC curve of 0.73 denoting a predictive accuracy of 73%. Right ventricle diameter above 38 mm was found to be an independent predictor of adverse outcomes. These findings reiterate the prognostic value of echocardiography in these patients. All COPD patients with stable disease should undergo echocardiographic evaluation to determine prognosis.

Reference

1. Rizzatti FP, et al. Right ventricle diastolic diameter can be used as a predictor of adverse outcomes in COPD patients. *Am J Respir Crit Care Med*. 2023;207:A1147. Available at: https://doi.org/10.1164/ajrccm-conference.2023.207.1_MeetingAbstracts.A1147



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Lighter Side of Medicine

INSPIRATIONAL STORY

THE TOUCHSTONE

When the great library of Alexandria burned, the story goes, one book was saved. But it was not a valuable book; and so a poor man, who could read a little, bought it for a few coppers.

The book wasn't very interesting, but between its pages there was something very interesting indeed. It was a thin strip of vellum on which was written the secret of the "Touchstone"!

The touchstone was a small pebble that could turn any common metal into pure gold. The writing explained that it was lying among thousands and thousands of other pebbles that looked exactly like it. But the secret was this: The real stone would feel warm, while ordinary pebbles are cold.

So the man sold his few belongings, bought some simple supplies, camped on the seashore, and began testing pebbles.

He knew that if he picked up ordinary pebbles and threw them down again because they were cold, he might pick up the same pebble hundreds of times. So, when he felt one that was cold, he threw it into the sea. He spent a whole day doing this but none of them was the touchstone. Yet he went on and on this way. Pick up a pebble. Cold - throw it into the sea. Pick up another. Throw it into the sea.

The days stretched into weeks and the weeks into months. One day; however, about mid-afternoon, he picked up a pebble and it was warm. He threw it into the sea before he realized what he had done. He had formed such a strong habit of throwing each pebble into the sea that when the one he wanted came along, he still threw it away.

So it is with opportunity. Unless we are vigilant, it's easy to fail to recognize an opportunity when it is in hand and it's just as easy to throw it away.

HUMOR

IDENTITY

A certain little girl, when asked her name, would reply, "I'm Mr Sugarbrown's daughter." Her mother told her this was wrong, she must say, "I'm Jane Sugarbrown."

The Vicar spoke to her in Sunday School and said, "Aren't you Mr Sugarbrown's daughter?"

She replied, "I thought I was, but mother says I'm not."

THREE THINGS HAPPEN

"As you get older three things happen. The first is your memory goes, and I can't remember the other two..."

—Sir Norman Wisdom

THE ANESTHESIOLOGIST

Jill received a bill from the hospital for her recent surgery, and was astonished to see a \$900 fee for the anesthesiologist. She called his office to demand an explanation. "Is this some kind of mistake?" Jill asked when she got the doctor on the phone. "No, not at all," the doctor said calmly.

"Well," said Jill, "that's awfully costly for knocking someone out." "Not at all," replied the doctor. "I knock you out for free. The 900 dollars is for bringing you back around."

Dr. Good and Dr. Bad

SITUATION: A type 2 diabetic individual was asked to get his iron and hemoglobin levels checked which were found to be high.



LESSON: It has been suggested that high levels of hemoglobin and iron are harmful for the kidney function among individuals with diabetes. In addition, it has been reported that HDL-C may play a role in the relation of high hemoglobin in kidney function in diabetic population.

J Diabetes Complications. 2017;31(6):958-63.



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Articles

Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

Articles in Books

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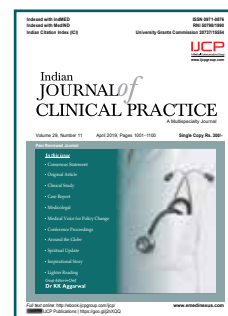
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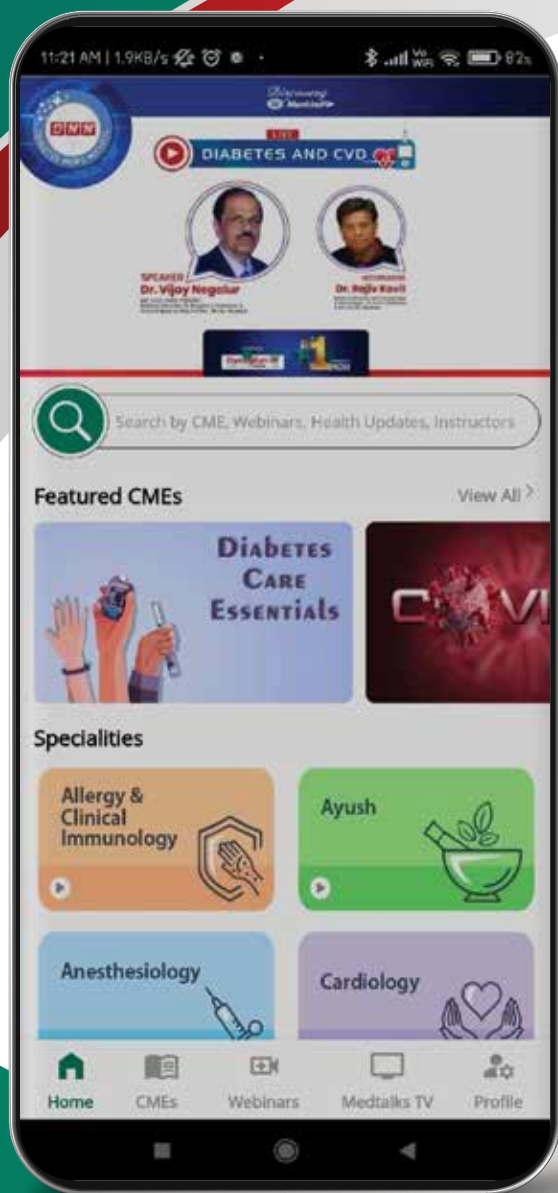
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Reference: 1. RYBELSUS[®] (package insert). Plainsboro, NJ: Novo Nordisk Inc; April 2021.

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