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## Coronavirus Updates

*Speaker: Dr Monica Vasudev Allergist and Clinical Immunologist, Fellow of American Academy of Asthma, Allergy and Immunology, Advocate Aurora Health, Wisconsin, USA*

### **WHO Approves Covovax Covid-19 Vaccine for Emergency Use**

The World Health Organization (WHO) has issued an emergency use listing (EUL) for Covovax "NVX-CoV2373" produced by the Serum Institute of India under licence from Novavax. Covovax requires two doses and is produced by creating an engineered baculovirus containing a gene for a modified SARS-CoV-2 spike protein. It is a subunit of the vaccine developed by Novavax and the Coalition for Epidemic Preparedness Innovations (CEPI) ... (Source: WHO, December 17, 2021)

### **More Than 5 Times Higher Risk of Reinfection with Omicron Than Delta**

New research from the Imperial College London has found that Omicron was associated with a 5.41-fold higher risk of reinfection compared with Delta suggesting that immunity accorded by previous infection is as low as 19%. Persons who had taken their second vaccine dose 2 or more weeks before and were 2 or more weeks past their booster dose were at an

increased risk of developing a symptomatic Omicron case compared to Delta ... (Source: Imperial College, Report 49, December 16, 2021)

### **Omicron May Become The Dominant Strain in Europe Early Next Year**

The European Centre for Disease Prevention and Control (ECDC) has stated that the "Omicron variant of concern (VOC) was likely to overtake Delta within the first 2 months of 2022". There is a very high-risk of it becoming the dominant strain in Europe because of its high transmissibility, although data is inadequate at this point of time to actually determine the severity of the infection caused by Omicron variant. Stella Kyriakides European Health Commissioner has expressed concern about the slow vaccination rates in countries like Bulgaria, Romania and Slovakia, where less than 50% of the population has been immunized... (Medscape, December 16, 2021)

### **The Next-Generation SARS-CoV-2 Vaccine**

The US Army has developed a spike ferritin nanoparticle vaccine, which is expected to protect from other respiratory viruses and not just SARS-CoV-2. The vaccine uses ferritin as a soccer ball-shaped "platform". It has 24 "faces" to which are attached the replicas of the spike proteins through which the virus enters the



cells. The vaccine would not require special storage as it is stable at varying temperatures. The first trial of the vaccine in humans has been completed and results are being evaluated. According to Gordon Joyce of the Walter Reed Army Institute of Research in Silver Spring, Maryland, the study lead author said, "*Presenting multiple copies of spike in an ordered fashion may be the key to inducing a potent and broad immune response.*" (Source: Medscape)

**Risk of Myocarditis After Adenovirus-Based Covid-19 Vaccine**

*Nature Medicine* has probably published the first report of risk of acute myocarditis with an adenovirus-vector vaccine. The incidence rate ratios (IRRs) for myocarditis 1 to 7 days after the first AstraZeneca, Pfizer, and Moderna injections were 1.76, 1.45, and 8.38, respectively,

and 23.1 after the second dose of the Moderna vaccine... (Source: Medscape, December 16, 2021)

**Compulsory Vaccination for Healthcare Workers in Germany**

Healthcare workers at hospitals, doctor's offices and nursing homes in Germany are now required by law to get the Covid-19 vaccine. They must prove that they are vaccinated or have recovered from COVID-19 by mid-March as part of new legislation passed by the parliament on Friday. The new legislation allows closure of bars and restaurants and banning of large gathering events. Health Minister Karl Lauterbach, "It's absolutely unacceptable that in establishments where people live, who put their trust in us to protect them, that people are unnecessarily dying because unvaccinated work there." ... (Medscape, December 13, 2021)



# Management of Diabetic End-stage Renal Disease: Role of Hemodialysis

H SUDARSHAN BALLAL

## ABSTRACT

Diabetes mellitus is now the most common cause of end-stage renal disease (ESRD) all across the globe, including India. In view of the alarming rise in numbers, renal failure due to type 2 diabetes has been termed a “medical catastrophe of worldwide dimensions.” When a patient develops uremic symptoms he needs renal replacement therapy. The renal replacement therapies available for all patients with ESRD are: hemodialysis, chronic ambulatory peritoneal dialysis (CAPD) and renal transplantation. Kidney transplantation is the best option for patients with diabetic ESRD. The 5-year survival of transplant patients of 75-85% is far superior to the 5-year survival rate of around 25% on dialysis.

**Keywords:** Diabetes mellitus, end-stage renal disease, renal replacement therapies, hemodialysis, CAPD, renal transplantation

Diabetes mellitus is now the most common cause of end-stage renal disease (ESRD) all across the globe, including India. It is estimated that 30-50% of patients being initiated on renal replacement therapy (RRT) have diabetes as the cause of their ESRD<sup>1</sup> and most of these patients have type 2 diabetes. In view of the alarming rise in numbers, renal failure due to type 2 diabetes has been termed a “medical catastrophe of worldwide dimensions”.<sup>2</sup> This article will discuss the management of diabetic ESRD specifically related to type 2 diabetes.

## RENAL REPLACEMENT THERAPY

When a patient’s kidney function, as measured by the calculated glomerular filtration rate, has reached <10 mL/min (ESRD) or the patient develops uremic symptoms they need RRT.

The RRTs available for all patients with ESRD are:

- Hemodialysis
- Chronic ambulatory peritoneal dialysis (CAPD)
- Renal transplantation.

Though these modalities are available for all patients with ESRD, there are significant differences in the morbidity and mortality of any given modality between

the diabetic and nondiabetic ESRD population. We will discuss some of these issues, specifically the modality of hemodialysis.

## HEMODIALYSIS FOR DIABETIC ESRD

Although hemodialysis prevents death from uremia, the patient survival on hemodialysis is poor, especially for patients with diabetes, being approximately 20-25% at 5 years as compared to 40-50% for other causes of ESRD.<sup>3</sup> This is worse than many cancers. The survival of patients on maintenance hemodialysis in India seems dismal for both, diabetic and nondiabetic populations.<sup>4</sup>

The important contributors for mortality in the diabetic dialysis population are: Cardiovascular disease, adequacy of dialysis and nutritional status.

- **Cardiovascular disease (CVD):** CVD is the most common cause of death accounting for more than one-half of the cases.<sup>5</sup> The main reason for such a high mortality rate, which is of cardiovascular origin in the majority of cases is that the cardiovascular conditions of patients with diabetes are already severely impaired when they start RRT, as demonstrated by the high prevalence of coronary artery disease, stroke, peripheral occlusive disease and amputations. This also explains why patients who have diabetes and are on RRTs are at higher risk of developing *de novo* CVD, particularly ischemic heart disease, which not only is more frequent but also has a more aggressive course than in nondiabetic patients. In view of this, aggressive

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measures to manage CVD need to be adopted in all diabetic patients even before they reach the stage of dialysis.

- **Adequacy of dialysis:** Adequacy of dialysis, which also plays an important role in CVD and nutrition (MIA or malnutrition inflammation atherosclerosis syndrome), is also a contributor to the poor outcome and diabetics, in particular, seem to be more sensitive than nondiabetics to inadequate dialysis.<sup>6</sup> The increase in mortality of these patients largely disappears if there is an improvement in the nutritional status as reflected by an increase in serum albumin and creatinine.<sup>7</sup> This is a major problem in India where for various reasons like financial constraints, lack of access and availability of good dialysis units causes most patients to have inadequate dialysis.<sup>8</sup> Whenever possible, it is very essential to monitor the adequacy of dialysis by using biochemical measures like urea reduction rates, Kt/V and clinical well-being of patients and to take measures to improve the adequacy of dialysis.
- **Nutrition in dialysis:** Nutrition in dialysis patients is closely linked to inadequate dialysis, which

leads to anorexia and poor calorie and protein intake. This is reflected by poor serum albumin and creatinine levels, which are indicators for mortality in dialysis patients. The problems of diabetic gastroparesis and diabetic enteropathy compound the nutritional problems.

The help of a good dietician and measures to treat diabetic gastroparesis and enteropathy by motility agents, frequent small foods and appropriate use of broad-spectrum antibiotics to treat bacterial infections in diabetic enteropathy are needed to maintain adequate nutrition. It is to be noted that cisapride is best avoided in this population because of the risk of fatal arrhythmias.<sup>9</sup>

### DIET IN DIABETIC PATIENTS ON DIALYSIS

The general recommendation for diet in dialysis patients is given in Table 1. The iron requirement of dialysis patients varies and will need to be addressed on a patient to patient basis. In general, water-soluble vitamins are routinely prescribed and calcitriol may be needed in some patients.

**Table 1.** Daily Dietary Recommendations for Dialysis Patients versus Nonuremics<sup>a</sup>

Factor	Nonuremic	HD	PD
Protein (g/kg)	0.8	1.2	1.2-1.5
Calories (sedentary; kcal/kg)	30	30 <sup>b</sup>	30-40 <sup>b,c</sup>
Protein (%)	15-20	15	15
Carbohydrate (%)	55-60	55-60 <sup>d</sup>	55-60 <sup>c,d</sup>
Fat (%)	20-30	Balance	Balance
Cholesterol (mg)	300-400	300-400	300-400
Polyunsaturated/Saturated fat ratio	2.0:1.0	2.0:1.0	2.0:1.0
Crude fiber (g)	25	25	25
Sodium (1 g = 43 mEq)	2-6 g	2 g + 1 g/LUO	2-4 g + 1 g/LUO
Fluids (L)	Ad lib 1 L/LUO	1 L + 1 L/LUO	1.0-2.5 L + 1 L/LUO
Potassium (1 g = 25 mEq)	2-6 g	2 g + 1 g/LUO	4 g + 1 g/LUO
Calcium (g)	0.8-1.2	Diet +1.2	Diet + 1.2
Phosphorus (g)	1.0-1.8	0.6-1.2	0.6-1.2
Magnesium (g)	0.35	0.2-0.3	0.2-0.3

<sup>a</sup>All intakes calculated on the basis of normalized body weight (i.e., the average body weight of normal persons of the same age, height and sex as the patient).

<sup>b</sup>These levels of caloric intake are rarely attained in practice.

<sup>c</sup>Includes glucose absorbed from dialysis solutions.

<sup>d</sup>Carbohydrate intake should be decreased in patients with hypertriglyceridemia.

HD = Hemodialysis; PD = Peritoneal dialysis; LUO = Liters of urine output per day.



## **BLOOD SUGAR CONTROL IN DIABETIC DIALYSIS PATIENTS**

There are certain special problems about blood sugar control in dialysis patients.

### **Altered Insulin Metabolism**

In uremic patients (both diabetic and nondiabetic), insulin secretion by the  $\beta$ -cells of the pancreas is reduced and the responsiveness of peripheral tissues (e.g., muscle) to insulin is depressed. On the other hand, the rate of insulin catabolism (renal and extrarenal) is decreased, and therefore, the half-life of any insulin present in the circulation is prolonged.

All of these abnormalities are only partially corrected after institution of maintenance dialysis therapy.

### **Increased Sensitivity to Insulin**

In diabetic dialysis patients treated with exogenous insulin, the importance of reduced insulin catabolism overrides the impact of insulin resistance; when exogenous insulin is administered, its effect may be intensified and prolonged. Thus, smaller than usual doses should be given.

### **Insulin Therapy**

Tight control of sugar is sometimes difficult to achieve in diabetic dialysis patients. Nevertheless, good glucose control is worthwhile with split doses of insulin preferably. The "amount of insulin" per day required for patients receiving maintenance hemodialysis is usually small; optimum control of glycemia is achieved by administration of long-acting insulin at two separate times during the day (split dosing) and by supplementing with regular insulin for meals as needed. The proportions of long-acting and regular insulin, as well as the total insulin doses vary widely among different patients. Hypoglycemia is quite common in diabetic dialysis patients usually due to reduced insulin catabolism and reduced intake or food and/or poor absorption.

A fasting serum glucose of <140 mg/dL and a postprandial value <200 mg/dL is a reasonable goal to achieve.

### **Oral Hypoglycemic Agents**

Lack of clinical studies on use of oral hypoglycemic agents (OHAs) in dialysis patients restricts the use of these agents.

Nevertheless, these agents are useful adjuncts in the treatment of diabetics and are used by many

nephrologists. The safety of sulfonylureas depends on their mode of metabolism and their half-life. Use of short-acting agents primarily metabolized by the liver is, in general, safer in dialysis patients. Acetohexamide, chlorpropamide and tolazamide are excreted to a large extent in the urine. These drugs should not be used in dialysis patients because their half-lives will be greatly prolonged in the absence of renal function, possibly resulting in severe and prolonged hypoglycemia. The excretion of glyburide is 50% hepatic, and prolonged hypoglycemia has been reported using this drug in dialysis patients. Metabolism of glipizide, tolbutamide and gliclazide is almost completely hepatic. Consequently, the last three drugs should be considered if an OHA is desired. Many drugs frequently used in dialysis patients either antagonize (phenytoin, nicotinic acid, diuretics) or enhance (sulfonamides, salicylates, warfarin, ethanol) the hypoglycemic action of sulfonylureas.

Metformin, a biguanide, is associated with increased incidence of lactic acidosis in dialysis patients and should not be used. Acarbose inhibits  $\alpha$ -glucosidase in the enteric mucosa and moderates postprandial hyperglycemia. It may prove to be a useful adjunct to other diabetic medications in diabetic patients. Troglitazone and other thiazolidinediones sensitize the target tissues to insulin and may be of help in obese, type 2 diabetics with insulin resistance. However, the use of this class of drugs may be associated with the risk of severe hepatotoxicity.

In general, insulin use is preferable in diabetic dialysis patients but judicious use of appropriate OHAs can be done.

Specific problems of hemodialysis in diabetic patients:

- Difficulty in creating and maintaining a vascular access because of severe peripheral vascular disease (PVD) in older diabetic patients.
- Inability to tolerate volume shifts giving rise to hypotension during hemodialysis because of autonomic neuropathy and CVD.
- Risk of infection.
- Progression of diabetic retinopathy.

In view of all these problems, meticulous planning and appropriate management should start in the predialysis period well before dialysis is anticipated and would involve a special diabetic team consisting of an Ophthalmologist, Vascular Surgeon, Podiatrist, Endocrinologist, Cardiologist, Neurologist and Dietician to help the nephrology team in keeping the patient as fit as possible even before they reach dialysis.

### TIMING OF DIALYSIS IN DIABETIC ESRD

In general, most nondiabetic patients are initiated on dialysis when the creatinine clearance is <10 mL/min.

In diabetic patients, dialysis may have to be initiated at creatinine clearance even >15 mL/min.<sup>9</sup> The reasons for this being:

- ⦿ Renal functions deteriorate rapidly in this group
- ⦿ Hypertension is very difficult to control with severe renal failure
- ⦿ Most patients have CVD with volume overload
- ⦿ Uremic symptoms may manifest earlier than non-diabetic patients.

In spite of these recommendations, dialysis is usually started as an emergency in most Indian patients because of uremia, pulmonary edema or severe hyperkalemia because of poor awareness, financial constraints and lack of facilities for dialysis.<sup>4,8</sup>

### ROLE OF CAPD

CAPD is another modality of treatment in diabetic ESRD. Though it has its advantages and disadvantages, the following factors decide the modality of dialysis:

- ⦿ Comorbid conditions
- ⦿ Family and home support
- ⦿ Financial support
- ⦿ CVD and PVD leading to poor vascular access for dialysis
- ⦿ Hemodynamic stability
- ⦿ Availability of hemodialysis centers.

CAPD is 30-50% more expensive than hemodialysis in India and is generally used for patients who do not have access to hemodialysis, have severe chronic heart failure (CHF), hemodynamic instability, poor vascular access and are not candidates for transplantation. The patient and the family should be motivated and have adequate financial support. Table 2 gives the comparison between the two modalities of dialysis.

**Table 2.** Dialysis Modalities for Diabetics

Modality	Advantages	Disadvantages
<b>Hemodialysis</b>	Very efficient	Risky for patients with advanced cardiac disease
	Frequent medical follow-up (in center)	Multiple arteriovenous access surgeries often required; risk of severe hand ischemia
	No protein loss to dialysate	High incidence of hypotension during dialysis session Predialysis hyperkalemia Prone to hypoglycemia
<b>CAPD</b>	Good cardiovascular tolerance	Peritonitis, exit site and tunnel infection risks similar to those in nondiabetic dialysis patients
	No need for arteriovenous access	Protein loss to dialysate
	Good control of serum potassium	Increased intra-abdominal pressure effects (hernias, fluid leaks, etc.)
	Good glucose control, particularly with use of intraperitoneal insulin; less severe hypoglycemia	Schedule not convenient for helper if one is required (e.g., for a patient with physical disability like blindness, stroke, etc.)
<b>CCPD</b>	Good cardiovascular tolerance	Protein loss to dialysate
	No need for arteriovenous access	
	Good control of serum potassium	
	Good glucose control with use of intraperitoneal insulin	Very very expensive
	Good for patients with disability Peritonitis risk slightly less than for CAPD	

CAPD = Continuous ambulatory peritoneal dialysis; CCPD = Continuous cycling peritoneal dialysis.

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## **SURVIVAL ON HEMODIALYSIS AND PERITONEAL DIALYSIS**

There have been conflicting data about the survival of patients on CAPD compared to hemodialysis. Initial data from Michigan suggested an advantage for CAPD.<sup>10</sup> However, most studies after adjustment for comorbid condition, have not found a statistically significant survival difference between the two modalities.<sup>11</sup>

## **TRANSPLANTATION**

Kidney transplantation is the best option for patients with diabetic ESRD. The 5-year survival of transplant patients of 75-85%, though less than that of nondiabetic ESRD, is still far superior to the 5-year survival rate of around 25% on dialysis.<sup>3,12</sup> Though in general healthier patients go on to transplant and sicker patients remain on dialysis the survival rates are better, even when these are factored in. Transplantation is also associated with a better quality-of-life and high degree of rehabilitation.

The pre- and post-transplant care of diabetic patients is generally similar to that of nondiabetics. However, in view of the high prevalence of CVD in this population, meticulous attention has to be paid to screen these patients for CVD prior to the transplantation.<sup>13</sup>

## **RECOMMENDATIONS FOR TREATMENT OF DIABETIC ESRD PATIENTS**

Kidney transplant remains the best option of RRT for patients with diabetic ESRD in all suitable candidates. Recommendations for those not suitable for transplantation-

CAPD is recommended for patients with:

- Poor vascular access because of PVD
- Severe CVD with hemodynamic instability during hemodialysis
- Nonavailability of hemodialysis centers
- Good family and financial support
- Motivated patients.

Hemodialysis is the treatment for all the rest which is the treatment available for the vast majority of patients with diabetic ESRD in India who are not candidates for transplantation. In view of the multiple associated comorbid conditions, a multidisciplinary approach

is needed to prevent and manage the complications of vascular diseases, malnutrition and retinopathy in diabetic dialysis patients.

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## CLINICAL STUDY

# Predicting Clinical Outcome in Diabetics versus Nondiabetics with Acute Myocardial Infarction After Thrombolysis

AMGOOTH BANU PRIYA\*, ARUN PRASATH\*, C RAMAKRISHNAN†, SM RAJENDRAN‡

### ABSTRACT

Acute myocardial infarction can be considered as a potential epidemic for mankind (WHO 1982). Diabetes mellitus is one of the 6 primary risk factors identified for myocardial infarction. The aim of our study was to correlate the incidence of complications with diabetes by using ST segment resolution as a tool, thereby re-enforcing the role of incomplete ST resolution as a marker of worse clinical outcome in cases of diabetes with ST-elevated myocardial infarction in our population.

**Keywords:** Acute myocardial infarction, thrombolysis, ST segment elevation, reperfusion

The acute coronary syndrome includes unstable angina, non-ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI). Diabetes mellitus is one of the 6 primary factors identified for myocardial infarction (MI), others being dyslipidemia, smoking, male gender, hypertension and family history of atherosclerotic arterial disease. Diabetes mellitus is a metabolic disorder which increases the rate of atherosclerosis progression of vascular occlusion.<sup>1</sup> Even after prompt thrombolysis, the aftermath of diabetic patients is still worse than the nondiabetics, indicating impaired post-thrombolysis left ventricular function and prognosis.

The aim of thrombolysis in acute MI is early and complete myocardial reperfusion.<sup>2</sup> Incomplete or failed reperfusion is associated with increased risk of complications. Analysis of ST segment resolution on electrocardiogram (ECG), after fibrinolytic therapy, in

cases of STEMI, offers an attractive and cost-effective solution to assess coronary reperfusion. Whereas coronary angiogram is a marker for epicardial reperfusion, ST segment resolution offers a better reflection of microvascular reperfusion. Although successful thrombolysis of the epicardial vessel is necessary for good prognosis, but the microvascular flow more strongly correlates with the outcome. ST segment is, therefore, a better indicator of prognosis, and provides information, which cannot be assessed on basis of coronary angiogram alone.<sup>3,4</sup> In fact, Schröder et al,<sup>5</sup> reported that absence of ST segment resolution was the most powerful independent predictor of early mortality ( $p = 0.0001$ ).

ST resolution can also be used as a tool to identify candidates for early invasive procedures such as percutaneous transluminal coronary angioplasty (PTCA), who are at risk of developing complications because of nonresolution of ST segment after initial thrombolytic therapy.<sup>6</sup> Since, ECG is widely available even in developing nations, it is important to establish its effectiveness as a tool for assessing reperfusion as it will offer the cheapest alternative for assessing recovery and myocardial salvage.

### MATERIAL AND METHODS

The prospective study was conducted at Sree Balaji Medical College and Hospital, Chennai from June 2015 to October 2015. All cases of acute MI with the

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diagnosis based on the World Health Organization (WHO) criteria i.e., presence of any 2 of the following were included.

- Chest pain consistent with acute MI of less than 24 hours duration.
- Electrocardiography changes i.e., ST segment elevation >0.2 mV in at least 2 contiguous chest leads or >0.1 mV in at least 2 contiguous limb leads.
- New or presumably new left bundle branch block on ECG.
- Raised levels of cardiac enzymes creatine phosphokinase-MB more than double of the reference value or positive troponin I test done with commercially available kits of trop I.

These patients came within 12 hours of chest pain and received streptokinase on presentation. Patients coming after 12 hours of chest pain and patients suffering from type 1 diabetes mellitus were excluded.

The study population was divided into two groups: Group A, nondiabetics (n = 50) and Group B, diabetics (n = 50). Only those patients who were known cases of diabetes or in whom it was established during hospital stay by repeated blood glucose estimation, were included in Group B.

A detailed history was taken, particularly of age, sex, occupation, address, history of smoking, diabetes mellitus, hypertension and family history of ischemic heart disease. Complete physical examination of patients was done upon presentation in emergency and important parameters such as pulse and blood pressure were noted. Patients were followed up daily. Pulse, ECG changes and complications, if any, were monitored till death or discharge of the patient. The endpoint was a composite of recurrent ischemic chest pain, heart failure, arrhythmia or death.

Time from onset of chest pain to presentation of patient in emergency was noted through the history. ECG recordings of patients were taken upon presentation in emergency. ST elevation was recorded in millimeters from the lead in which maximum elevation was observed. Injection streptokinase was given intravenously to each patient at a dose of 1.5 million units, diluted in 100 mL of normal saline, in 1 hour.

Repeat ECG was performed after 60 minutes of administration of streptokinase (SK). ST resolution was observed in the lead with the maximum ST elevation. ST resolution was defined as a reduction of >50% ST segment elevation after thrombolysis. Informed written

consent of the patient/attendant was taken. Follow-up was conducted for each patient throughout his/her hospital stay. Fasting plasma glucose (FPG) was recorded from all patients, in the morning of day following hospital admission for differentiating new cases of diabetes, stress hyperglycemia and nondiabetic. FPG measurements were repeated in stable condition prior to discharge from hospital.

The patients were also assessed for the complications during the follow-up. The major complications assessed were: Recurrent ischemic chest pain, heart failure, arrhythmia and death. Recurrent ischemic chest pain was assessed on the basis of history and ECG; heart failure was assessed on the basis of clinical examination, chest X-ray and echocardiography. Arrhythmia was evaluated on the basis of continuous bedside monitoring of ECG. Tachycardia was defined as pulse rate >100 and bradycardia as ≤50/min.

### Statistical Analysis

All data was analyzed by SPSS (statistical package for social sciences) version 12.0 for windows, chi-square test was used to compare the demographic characteristics and completion in both groups with 0.05% level of significance.

### RESULTS

A total of 100 patients were investigated in this study, of which 70 (70%) were males and 30 (30%) were females. Table 1 shows the demographic characteristics of the study population at presentation. There was no significant difference in the comorbidities of the two groups with hypertension showing the most significant trend.

**Table 1. Demographic Data at Time of Presentation**

Demographic characteristics	Nondiabetic (Group A) (n = 50)	Diabetic (Group B) (n = 50)
Mean age	55.34 ± 14.38	58.30 ± 12.26
Gender		
Male	38 (76%)	32 (64%)
Female	12 (24%)	18 (36%)
Time of thrombolysis in hours	5.88 ± 1.0	5.07 ± 1.3
Hypertension	15 (30%)	26 (52%)
Hypercholesterolemia	10 (20%)	10 (20.2%)
Family history	9 (18.2%)	7 (14.8%)
Smoking	25 (50%)	24 (48%)



## DISCUSSIONS

The time to reperfusion and complete reperfusion remain the key determinants for fibrinolysis. Historically, ST resolution has been one of the markers used to assess reperfusion in STEMI. Its importance cannot be denied as a prognostic indicator and the results of our study also reinforce this fact. However, its use as a cost-effective marker has been underutilized. Several studies have reported similar angiographic<sup>7,8</sup> or ECG<sup>9,10</sup> success in both type 2 diabetic and nondiabetic subjects, while others have shown that the diabetics have less complete resolution of ST elevation than the nondiabetics.<sup>11</sup> To evaluate this issue, it has been hypothesized that type 2 diabetes might interfere with intravenous thrombolysis effectiveness, as estimated by angiographic or ECG criteria.

In our study, we observed that in nondiabetic MI 84% patients showed complete resolution and 16% showed failed resolution. But in case of diabetic MI, 13.8% patients showed complete resolution and 86% showed failed resolution. In our study, more complete ST resolution was seen in nondiabetic patient (84% vs. 16%,  $p < 0.001$ ), whereas type 2 diabetic subjects presented with significantly higher incidence of failed ST resolution than nondiabetic subjects (88% vs. 14.8%,  $p < 0.001$ ). This significant change in ST resolution between nondiabetic and diabetic group was similar with the study, which showed significant difference between nondiabetic and diabetic patients in relation to complete (35.1% vs. 69.2%,  $p < 0.001$ ) and incomplete (66.8% vs. 32.6%,  $p < 0.001$ ) resolution.<sup>11</sup> Our results are also consistent with a published meta-analysis in which it was shown that type 2 diabetic subjects had less ST resolution after intravenous thrombolysis administration compared with nondiabetic subjects.<sup>7</sup>

Our results showed the frequency of complications in nondiabetics to be 32.9% compared to 79.8% in diabetics ( $p < 0.001$ ), which was substantially higher in the latter. This finding, therefore establishes a direct correlation between diabetics and the frequency of complications, reflected by less complete ST segment resolution in diabetics in our study (86%).

In our study, we noted that there was a significant interaction between diabetic status and failed ST resolution with respect to the occurrence of in-hospital recurrent ischemia ( $p < 0.0001$ ). Recurrent chest pain is the most common complication observed in the study. A study supporting our results showed that there was a significant interaction between diabetics status and treatment strategy with respect to the occurrence of

in-hospital recurrent ischemia.<sup>12</sup> In that study, 32.5% diabetics and 22.1% nondiabetics developed recurrent ischemia after fibrinolysis ( $p < 0.001$ ). As shown by another study, diabetic patients may have a greater residual lesion in the infarct-related artery after treatment with fibrinolytics, resulting in a higher rate of recurrent ischemia.

In our results, we observed that the interaction between diabetics status and failed ST resolution with respect to the development of heart failure was significant ( $p = 0.025$ ). Heart failure is the major determinant for prognosis after MI. Since, some patients never had an echocardiography before this hospital admission to rule out prior heart failure, so any indication of heart failure post-thrombolysis was considered a new development. Our results are supported by the findings of a study, which showed that in-hospital heart failure was more common among diabetics after fibrinolysis.<sup>12</sup> In that study, 10% diabetics and 4.2% nondiabetics developed heart failure ( $p = 0.001$ ).

We observed arrhythmias in 56% of diabetic patients as compared to 10% in nondiabetic patients ( $p < 0.0001$ ). The results clearly show that arrhythmias are less frequent in nondiabetic patients. Failed ST segment resolution was associated with high frequency of occurrence of arrhythmias compared with complete resolution of both diabetics ( $p < 0.0001$ ) and nondiabetics ( $p < 0.0001$ ). Our results are supported by a study in which incidence of AV block and LBBB, detected in half of the dying patients, was 3 times more common in diabetics than in nondiabetics subjects.

In our study, mortality in diabetic group (only patients with failed ST resolution) was 6.4% compared to 0% in nondiabetic group ( $p = 0.014$ ). A study supporting these findings was carried out by Timmer et al. According to their results, diabetes was associated with increased 30-day mortality. Diabetic mortality was 12.4% and nondiabetic mortality 6.9% after thrombolysis at 30-day endpoint. Small sample size of this study limits our conclusions. There was no post-hospital follow-up, so that is another weak factor of this study. Since, the hospital is equipped to deal with life-threatening emergencies, in-hospital death as a complication was not that high in any group.

The negative influence of diabetes on outcome after STEMI has been described previously. Because mortality remains particularly high in patients with diabetes after STEMI, it is important to define optimal treatment strategies including method of reperfusion therapy, in this population. In our study, it was proved

that reperfusion failed in a significant proportion of diabetic patients with STEMI in comparison with nondiabetic persons (86% vs. 16%). Similar results were obtained by Zairis et al.<sup>11</sup> They proved that fibrinolysis may be less effective in diabetic patients. Angeja et al<sup>7</sup> showed that microvascular flow is decreased in diabetic patients after fibrinolysis. Possibly, this is associated with increased platelet aggregation and reduced ability to induce endothelium-mediated vasodilation.

The higher risk of adverse events may be caused by enhanced thrombogenicity and impaired fibrinolysis. Percutaneous coronary intervention (PCI) can be a better alternative in diabetics presenting with acute MI. However, the long-term outcome of these patients depends on the extent of coronary disease and residual left ventricular function, as well as the presence of other risk factors. Hence, aggressive secondary preventive measures such as tight glycemic control and lipid-lowering may be just as important as the mode of reperfusion treatment for these patients.

So, due attention is required for the better management of diabetic MI patients. This should, however, be supplemented with further therapies and strategies directed towards the many abnormalities that are associated with diabetes, such as endothelial dysfunction, dysglycemia and coagulation and fibrinolytic disturbances.

Our study was limited by the fact that the prognosis after STEMI is affected by various factors such as age, gender, number of coronary risk factors presented by the patient, use of aspirin within 7 days and number of angina attacks the patient suffered. We could not assess these factors, which correlate strongly with mortality in our study. A multivariate analysis is required to exclude the importance of these confounding factors.

Stress hyperglycemia has a detrimental effect on thrombolytic outcome after acute MI. Diabetes can be differentiated from stress hyperglycemia with certainty only after the acute phase of the infarction. Thus, any attempt to identify undiagnosed diabetes in our study would have been biased because patients must survive the acute phase to be diagnosed. Another limiting factor was the nonrandomized nature of the research and small size of patients included in the study. In addition to this, it was also limited by the fact that it was a single center study.

## CONCLUSION

Frequency of in-hospital complications is more in failed ST resolution compared to complete ST resolution, in

both diabetics and nondiabetics, post-thrombolysis. Diabetic population, after thrombolytic therapy, has a higher incidence of adverse clinical outcomes than nondiabetics. Among diabetic patients with acute MI, fibrinolysis was associated with less complete ST segment resolution, suggesting impaired microvascular flow. Abnormal microvascular flow may contribute at least in part to the poorer outcomes observed in patients with diabetes and acute MI.

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## CLINICAL STUDY

# Vitamin B<sub>12</sub> Levels in Patients with Type 2 Diabetes Mellitus on Metformin

V PADMA\*, NN ANAND\*

### ABSTRACT

Vitamin B<sub>12</sub> is required for proper hematopoiesis, cardiovascular and neurocognitive function. Vitamin B<sub>12</sub> deficiency is highly prevalent among patients with type 2 diabetes mellitus (T2DM) on metformin therapy. **Aim:** This study was carried out to evaluate the serum levels of vitamin B<sub>12</sub> in patients with T2DM on metformin therapy. **Material and methods:** Hundred patients with T2DM within the age group of 45-80 years were recruited into this cross-sectional study. All the patients were on metformin therapy for a minimum of 5 years. **Results:** Vitamin B<sub>12</sub> deficiency and borderline deficiency observed were 10.6% and 29% and 60.4% did not have vitamin B<sub>12</sub> deficiency. B<sub>12</sub> levels were lower in patients with more than 10 years of duration of diabetes and was statistically significant with a p value of 0.004. The average B<sub>12</sub> levels in patients on metformin dose of >1,000 mg was 349 pg/dL and in patients with metformin dose above 1,000 mg was 215 pg/dL. The difference between the two groups was statistically significant with a p value of <0.002. **Conclusion:** There is a high prevalence of B<sub>12</sub> deficiency among diabetic patients. It is important to screen for vitamin B<sub>12</sub> deficiency before initiating metformin and later annually.

**Keywords:** Vitamin B<sub>12</sub> deficiency, diabetes mellitus, peripheral neuropathy, metformin

Vitamin B<sub>12</sub> is an essential micronutrient required for proper hematopoiesis, cardiovascular and neurocognitive function. Biochemical and clinical vitamin B<sub>12</sub> deficiency is highly prevalent among patients with type 2 diabetes mellitus (T2DM) on metformin therapy. B<sub>12</sub> deficiency presents with a variety of clinical manifestations like megaloblastic anemia, pancytopenia, impaired memory, dementia, peripheral neuropathy and subacute combined degeneration of the spinal cord.

Metformin is the most commonly prescribed antidiabetic drug in patients with T2DM and is a cornerstone in the treatment of T2DM. It is well-tolerated in most of the patients.

Due to the numerous benefits of metformin, some side effects are usually ignored and rarely investigated. One such side effect is vitamin B<sub>12</sub> deficiency.

Vitamin B<sub>12</sub> or cobalamin plays an important role in DNA synthesis, hematopoiesis and neurological function. Vitamin B<sub>12</sub> deficiency is associated with hematological and neurocognitive dysfunction.<sup>1</sup> This study was hence carried out to evaluate the serum levels of vitamin B<sub>12</sub> in patients with T2DM on metformin therapy.

### MATERIAL AND METHODS

A total of 100 patients with T2DM within the age group of 45-80 years were recruited into this cross-sectional study. All the patients recruited were on metformin therapy for a minimum of 5 years.

### Exclusion Criteria

Patients with gastrectomy, small bowel resection, recent intake of vitamin B<sub>12</sub>, liver disease, chronic kidney disease and thyroid disease, patients on histamine 2 receptor blockers and vegetarians were excluded from this study. Participants were enrolled into this study after obtaining a written informed consent from each one of them.

Determination of serum vitamin B<sub>12</sub> level was by using high performance liquid chromatography (HPLC). Vitamin B<sub>12</sub> deficiency was defined as serum

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concentration of <200 pg/dL and borderline deficiency as 200-300 pg/dL. Concentrations >300 pg/dL were considered as normal. Statistical analysis was done using SPSS (Version 20.0) and the results were analyzed.

### RESULTS

Vitamin B<sub>12</sub> deficiency and borderline deficiency observed were 10.6%, 29% and 60.4% did not have vitamin B<sub>12</sub> deficiency.

Most of the patients were between the ages of 50-59 years - 39%, followed by >60 years - 25%, 40-49 years - 24% and 30-39 years - 12% (Fig. 1). Of them, 62% were females and 48% were males. The patients were divided according to the duration of diabetes into two groups: less than 10 years and more than 10 years of diabetes mellitus. The characteristics of patients with duration of therapy with metformin and B<sub>12</sub> levels are shown in Table 1.

The difference between B<sub>12</sub> levels in patients below 10 years of duration of diabetes and more than 10 years of duration of diabetes was statistically significant with a p value of 0.004.

### B<sub>12</sub> Levels and Metformin Dose

Forty-six percent of patients were on a dose of <1,000 mg of metformin per day and 54% were on a dose of >1,000 mg of metformin per day. The average B<sub>12</sub> levels in patients on metformin dose of <1,000 mg was 349 pg/dL and the levels in patients with metformin dose above 1,000 mg was 215 pg/dL (Fig. 2). The difference between the two groups was statistically significant with a p value of <0.002.

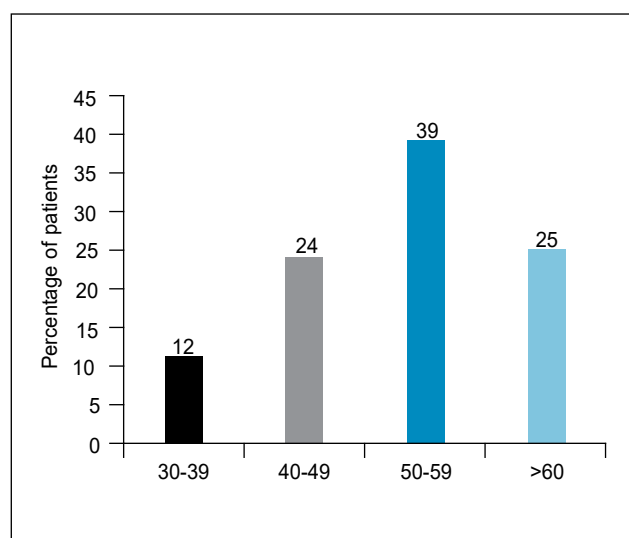


Figure 1. Diabetics on metformin.

Table 1. Characteristics of the Patients Including Levels of B<sub>12</sub> According to Duration of Diabetes

Characteristics	<10 years	>10 years
Age	54 ± 34	57 ± 51
BMI	25.62 ± 4	26.64 ± 32
Systolic BP	134 ± 14.24	136 ± 16.52
Diastolic BP	82 ± 11.22	84 ± 11.24
B <sub>12</sub> levels (pg/dL)	422.34	224.21

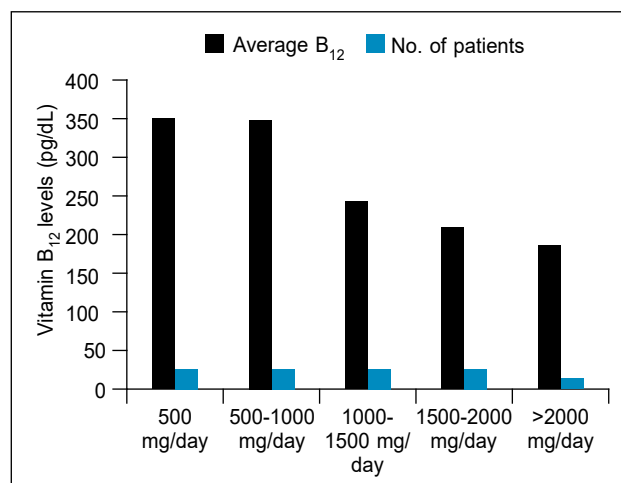


Figure 2. Average B<sub>12</sub> levels in patients according to dosage of metformin.

### DISCUSSION

Reports have shown that long-term metformin use has a significant impact on the concentration of vitamin B<sub>12</sub> in patients with T2DM.

Vitamin B<sub>12</sub> or cobalamin plays an important role in DNA synthesis, hematopoiesis and neurological function. Vitamin B<sub>12</sub> deficiency is associated with hematological and neurocognitive dysfunction.<sup>1</sup>

The source of vitamin B<sub>12</sub> is animal proteins. Vitamin B<sub>12</sub> deficiency is due to insufficient dietary intake among alcoholics and vegetarians, malabsorption due to chronic atrophic gastritis, pernicious anemia, chronic pancreatitis, celiac disease and drugs like metformin and proton pump inhibitors.

Vitamin B<sub>12</sub> deficiency results in disruption of the methylation process and increased accumulation of intracellular and serum homocysteine. Hyperhomocysteinemia has toxic effects on neurons and the vascular endothelium. This methylation reaction is essential in the conversion of dietary folate to its active metabolic form, tetrahydrofolate. Vitamin B<sub>12</sub> is the co-factor that mediates the conversion of methylmalonyl

coenzyme A (CoA) to succinyl-CoA. Vitamin B<sub>12</sub> deficiency leads to increase in serum methylmalonic acid (MMA), causing defective fatty acid synthesis of the neuronal membranes.<sup>2</sup> Vitamin B<sub>12</sub> is also essential in the synthesis of neurotransmitters like serotonin and dopamine.<sup>3</sup> Deficiency of dopamine and serotonin occurs with vitamin B<sub>12</sub> deficiency, which is the cause of the neurocognitive or psychiatric manifestations. Axonal demyelination, degeneration and later death due to vitamin B<sub>12</sub> deficiency manifests as severe peripheral or autonomic neuropathy, subacute combined degeneration of the spinal cord, dementia and delirium.<sup>4</sup> Hyperhomocysteinemia due to its cellular and vasculotoxic effects, is also associated with an increased risk of cardiovascular events.<sup>5</sup> Several cross-sectional studies<sup>6</sup> and case reports<sup>7</sup> have demonstrated an increased frequency of vitamin B<sub>12</sub> deficiency among T2DM patients. Metformin use has been demonstrated as the main factor associated with vitamin B<sub>12</sub> deficiency among patients with T2DM.<sup>8</sup> Studies on type 2 diabetic patients on metformin intake have demonstrated that the prevalence of vitamin B<sub>12</sub> deficiency is from 5.8% to 33%.<sup>9</sup> In a study by Qureshi et al,<sup>9</sup> a high prevalence of vitamin B<sub>12</sub> deficiency of 33% was seen in adult patients with T2DM.

### Metformin-induced Vitamin B<sub>12</sub> Deficiency Among Patients with T2DM

In a randomized controlled trial by DeFronzo et al, metformin reduced the serum vitamin B<sub>12</sub> levels by 22% and 29% when compared to glyburide and placebo, respectively.<sup>10</sup> The risk of developing metformin associated vitamin B<sub>12</sub> deficiency is increased by age, metformin dose and duration of treatment.<sup>11</sup> In a case-control study done in China among 155 adult Chinese diabetic patients on metformin and 310 controls, for every 1 g/day increase in metformin there was an odds ratio (OR) of 2.9 (95% confidence interval [CI], 2.15-3.87) for developing vitamin B<sub>12</sub> deficiency. Among patients treated with metformin for ≥3 years, the adjusted OR was 2.4 (95% CI, 1.46-3.91) when compared with diabetic patients who received metformin for ≤3 years.<sup>11</sup>

Decrease in vitamin B<sub>12</sub> absorption following metformin use starts as early as the 4th month of treatment.<sup>12</sup> Clinical features of vitamin B<sub>12</sub> deficiency develop only by 5-10 years, as there are a large amount of B<sub>12</sub> stores in the body (liver), which do not get depleted that fast.<sup>13</sup>

The mechanisms to explain metformin-induced vitamin B<sub>12</sub> deficiency in patients with T2DM are:

- Alterations in small bowel motility which stimulates bacterial overgrowth and vitamin B<sub>12</sub> deficiency
- Competitive inhibition of vitamin B<sub>12</sub> absorption
- Alterations in intrinsic factor (IF) levels
- Interaction with the cubulinendocytic receptor<sup>13</sup>
- Inhibition of the calcium-dependent absorption of the vitamin B<sub>12</sub>-IF complex at the terminal ileum (This inhibitory effect is reversed with calcium supplementation).<sup>14</sup>

Vitamin B<sub>12</sub> deficiency in patients with type 1 diabetes mellitus (T1DM) are due to:

- Pernicious anemia due to chronic autoimmune gastritis is high among patients with T1DM, more than 3 to 5 folds when compared to general population.<sup>15</sup>
- Exhibit autoantibodies to intrinsic factor (AIF) type 1 and 2<sup>15</sup> and parietal cell antibodies (PCA)<sup>16</sup> especially those diabetic patients with glutamate decarboxylase-65 (GAD-65) antibodies and HLA-DQA1\*0501-B1\*0301 haplotype.<sup>17</sup>
- Autoimmune hypothyroidism, celiac diseases are frequent comorbidities in patients with T1DM and they directly affect vitamin B<sub>12</sub> metabolism.<sup>18</sup> Dyserythropoiesis due to thyroid hormone deficiency, defective absorption due to reduced bowel motility, bacterial overgrowth and bowel wall edema also contribute to B<sub>12</sub> deficiency.<sup>18</sup>

Celiac disease is associated with enteropathy, chronic diarrhea and anemia due to malabsorption of folate and vitamin B<sub>12</sub>.<sup>19</sup>

## CONCLUSION

Clinical and biochemical vitamin B<sub>12</sub> deficiency is highly prevalent among patients with both T1DM and T2DM. As there is a high prevalence of B<sub>12</sub> deficiency among diabetic patients, it is clinically important to screen for vitamin B<sub>12</sub> deficiency before initiating metformin and later annually. Vitamin B<sub>12</sub> levels should be checked regularly among elderly patients with a history of long-term use of metformin (≥3-4 years), use of high doses of metformin (≥2 g/day), worsening diabetic distal polyneuropathy in the absence of other hematological abnormalities.<sup>20</sup> Vitamin B<sub>12</sub> levels <200 pg/mL is diagnostic of vitamin B<sub>12</sub> deficiency. Measurement of serum MMA or homocysteine concentrations is more sensitive and specific for screening type 2 diabetic patients with borderline serum vitamin B<sub>12</sub> concentrations of



200-400 pg/mL and mild-hematological manifestations. Normal levels of serum homocysteine and MMA concentrations are 5-15  $\mu\text{mol/L}$  and  $<0.28 \mu\text{mol/L}$ .<sup>20</sup> It is important to screen vitamin B<sub>12</sub> levels at diagnosis, then yearly for 3 years, then once in 5 years for life or if there are clinical signs of B<sub>12</sub> deficiency.<sup>15</sup>

Treatment of B<sub>12</sub> deficiency in adult patients with T2DM, intramuscular vitamin B<sub>12</sub> in doses of 1,000  $\mu\text{g}$  daily for a week, then weekly once for 4 weeks to correct vitamin B<sub>12</sub> deficiency. Associated folate deficiency should be treated with oral folate in doses of 5 mg daily for 1-4 months.

Large, well-designed studies have to be done in future on vitamin B<sub>12</sub> deficiency screening in diabetic patients and optimal supplementation dose among type 1 and type 2 diabetic patients to formulate guidelines for care of diabetic patients.

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## OBSERVATIONAL STUDY

# Study of Demographic Profile, Comorbidities, Role of Hydroxychloroquine Prophylaxis and Outcomes of COVID-19 Positive Healthcare Workers at a Tertiary Care Center in Southern Rajasthan

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### ABSTRACT

**Background:** In December 2019, a new respiratory tract infecting agent emerged in Wuhan city of China, known as the coronavirus. There are limited studies regarding coronavirus disease 2019 (COVID-19) in healthcare workers (HCWs). Therefore, the present study was aimed to determine the demographic profile, comorbidities, hydroxychloroquine as prophylaxis and outcomes of reverse transcription polymerase chain reaction (RT-PCR) confirmed COVID-19 HCWs. **Material and methods:** This study was an observational retrospective study carried out over a period of 10 months from 15th March, 2020 to 15th January, 2021 in 350 RT-PCR confirmed COVID-19 HCWs who were in home isolation or admitted in dedicated COVID hospital. **Results:** We observed that majority of HCWs were in the age group 20-39 years (66.58%), were males (69.14%) and from urban areas (72.86%). Only few had comorbidities (3.42%), took hydroxychloroquine as prophylaxis (5.71%) and mortality was 0.57%. About 46.29% of the HCWs were doctors and 28.40% of the doctors were from Medicine. **Conclusion:** From the present study, we conclude that HCWs affected by COVID-19 are mainly young adult male physicians from urban areas, without significant comorbidities. The outcome in COVID-19 positive HCWs is favorable due to better awareness, prompt diagnosis and treatment. The results of this study will be useful in knowing the most vulnerable section of HCWs.

**Keywords:** COVID-19, healthcare workers, hydroxychloroquine

In December 2019, a new respiratory tract infecting agent emerged in Wuhan city of China, known as the coronavirus. It was later named coronavirus disease 2019 (COVID-19). Full-genome sequencing and phylogenetic analysis indicated that 2019-nCoV is a form of beta-coronavirus which include human severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) viruses.<sup>1</sup> The World Health Organization (WHO) declared COVID-19 as a pandemic on 11th March, 2020, and from India, the

first case was reported on 30th January, 2020 from Kerala. Transmission of the coronavirus is usually via respiratory droplets in closed environments and through close contact between people and touching contaminated surfaces, with incubation period of 2-14 days and a reproductive number noted in early studies as 2.2.<sup>2</sup> COVID-19 has various clinical presentations that range from asymptomatic to mild symptoms such as fever, myalgia, sore throat, cough and cold to severe symptoms like acute respiratory distress syndrome, myocarditis, acute renal failure and multi-organ failure.<sup>3-5</sup>

According to WHO, healthcare workers (HCWs) are defined as all people engaged in actions whose primary intent is to enhance health.<sup>6</sup> In this pandemic, to manage COVID-19, many people came together and worked as HCWs.

In our study, HCWs included consultants and postgraduates from clinical as well as nonclinical departments, interns, undergraduate students, nursing staff, nursing students, paramedical staff and lab

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technicians. HCWs have exposure to COVID-19 patients directly or indirectly or to the infectious materials. Secondary transmission from HCWs is a possibility among patients, family members and the community.

Therefore, the present study was aimed to determine the demographic profile (age, sex, residence), comorbidities, role of hydroxychloroquine as prophylaxis and outcomes of reverse transcription polymerase chain reaction (RT-PCR) confirmed COVID-19 HCWs who were in home isolation or admitted in dedicated COVID hospital, a tertiary care institute attached to RNT Medical College, Udaipur, Rajasthan over a period of 10 months (15th March, 2020 to 15th January, 2021).

### AIMS AND OBJECTIVES

- To study the demographic profile (age, sex, residence) of COVID-19 positive HCWs.
- To study the comorbidities in COVID-19 affected HCWs.
- To study the role of hydroxychloroquine as prophylaxis in COVID-19 affected HCWs.
- To study the outcomes of COVID-19 positive HCWs.

### MATERIAL AND METHODS

This study was an observational retrospective study which was carried out over a period of 10 months from 15th March, 2020 to 15th January, 2021 in 350 RT-PCR confirmed COVID-19 HCWs who underwent home isolation or were admitted in dedicated COVID hospital, a tertiary care center attached to RNT Medical College, Udaipur, Rajasthan. We have analyzed the demographic profile, associated comorbidities, role of hydroxychloroquine drug as prophylaxis and outcomes of these HCWs.

#### Inclusion Criteria

All RT-PCR confirmed COVID-19 positive HCWs who were in home isolation or admitted in wards and intensive care unit (ICU) of our dedicated COVID hospital, irrespective of age and gender were included. HCWs included consultants and postgraduates from clinical as well as nonclinical departments, interns, undergraduate students, nursing staff, nursing students, paramedical staff and lab technicians.

#### Exclusion Criteria

HCWs who did not give written consent for the study.

### Methodology

HCWs who were suspected to be COVID-19 positive on the basis of their clinical history, contact history and travel history as per the Indian Council of Medical Research (ICMR) guidelines, underwent RT-PCR testing for COVID-19 and those who came out positive were admitted in COVID Dedicated Hospital (wards and ICU) or underwent home isolation and were enrolled in our study after written consent. The following parameters were used for our study:

- Demographic profile – which includes age-wise, sex-wise and area-wise distribution.
- Comorbidities – which include diabetes mellitus, hypertension, ischemic heart disease, chronic respiratory illness, malignancies and hypothyroidism.
- Number of HCWs taking hydroxychloroquine prophylaxis – which includes collecting information from the HCWs whether he or she had completed or was taking hydroxychloroquine as prophylaxis.
- Outcome was recorded in the form of recovery or deaths.
- Amongst the HCWs, we classified them into doctors, nursing staff, paramedical staff and lab technicians. We further divided the doctors department-wise to see the distribution of affected doctors in each and every department. This will further give us a better picture of the departments at risk of getting affected by COVID-19.

### OBSERVATION AND RESULTS

Table 1 shows the demographic profile in the COVID-19 positive HCWs. Among the age groups, maximum HCWs were in the 20-39 years group (66.58%) followed by 40-59 years age group (30.00%). Regarding gender, males were predominantly affected (69.14%). The disease predominantly involved the urban population (72.86%).

Table 2 shows the association of comorbidities with COVID-19 positive HCWs. Out of 350 HCWs, 12 had comorbidities (3.42%). Among comorbidities, diabetes mellitus was observed in maximum HCWs (1.42%), followed by hypertension (0.57%), chronic respiratory illness (0.57%), ischemic heart disease (0.28%), malignancy (0.28%) and hypothyroidism (0.28%).

Table 3 shows that out of the 350 HCWs affected, 20 took hydroxychloroquine prophylaxis (5.71%).

Table 4 shows the outcome of COVID-19 positive HCWs. Out of 350 HCWs, 348 got discharged (99.42%).

**Table 1.** Demographic Profile

Characteristics	HCWs (n = 350)	Percentage (%)
Age		
0-19 y	5	1.42
20-39 y	233	66.58
40-59 y	105	30.00
>60 y	7	2.00
Sex		
Male	242	69.14
Female	108	30.86
Residence		
Urban	255	72.86
Rural	95	27.14

**Table 2.** Comorbidities in COVID-19 Positive HCWs

Comorbidities	HCWs (n = 350)	Percentage (%)
Diabetes mellitus	5	1.42
Hypertension	2	0.57
Chronic respiratory illness	2	0.57
Ischemic heart disease	1	0.28
Malignancy	1	0.28
Hypothyroidism	1	0.28

**Table 3.** Number of HCWs Taking Hydroxychloroquine Drug as Prophylaxis

Hydroxychloroquine prophylaxis	HCWs (n = 350)	Percentage (%)
Yes	20	5.71
No	330	94.29

**Table 4.** Outcome of HCWs

Outcome	HCWs (n = 350)	Percentage (%)
Discharged	348	99.43
Death	2	0.57

Table 5 shows the distribution of COVID-19 positive HCWs. Out of 350 HCWs, maximum affected were doctors (46.29%) followed by nursing staff (37.14%), lab technicians (10.86%) and paramedical staff (5.71%). The table also shows the department-wise distribution of doctors. Among 162 doctors, maximum were from Medicine (28.40%) followed by Orthopedics (10.50%), Anesthesia (8.64%), Internship (8.64%), Pediatrics (7.40%), Surgery (6.80%), Obs and Gyne (6.17%),

**Table 5.** Distribution of COVID-19 Positive HCWs According to their Field

Subtypes	HCWs (n = 350)	Percentage (%)
Doctors	162	46.29
Medicine	46	28.40
Orthopedics	17	10.50
Anesthesia	14	8.64
Internship	14	8.64
Pediatrics	12	7.40
Surgery	11	6.80
Obs and Gyne	10	6.17
Radiodiagnosis	7	4.32
Biochemistry	4	2.47
ENT	4	2.47
Pathology	3	1.85
Anatomy	3	1.85
Microbiology	3	1.85
Physiology	3	1.85
PSM	3	1.85
Psychiatry	2	1.23
Ophthalmology	2	1.23
Radiotherapy	1	0.61
Dermatology	1	0.61
FMT	1	0.61
Dentist	1	0.61
Nursing staff	130	37.14
Paramedical staff	20	5.71
Lab technicians	38	10.86

Radiodiagnosis (4.32%), Biochemistry (2.47%), ENT (2.47%) and others.

## DISCUSSION

The present study was an observational retrospective study which was done over a period of 10 months (15th March, 2020 to 15th January, 2021) on 350 RT-PCR confirmed COVID-19 HCWs who underwent home isolation or were admitted in a dedicated COVID hospital attached to RNT Medical College, Udaipur, Rajasthan. These HCWs were analyzed in respect to demographic profile, comorbidities, role of hydroxychloroquine drug as prophylaxis and outcomes.

In the present study, we observed that COVID-19 affects all age groups. Out of 350 HCWs, maximum were from 20 to 39 years group (66.58%) followed by 40-59 years (30.00%), whereas the disease was less commonly



seen in >60 years (2.00%) and 0-19 years (1.42%) age groups. Lai et al and Sikkema et al also observed similar results and calculated median age of COVID-19 positive HCWs as 36.57 and 49 years,<sup>8</sup> respectively. The possible explanation of higher COVID-19 positivity in the age group 20-59 years (96.58%) may be due to the fact that this age group of HCWs may be actively involved in management of this pandemic. Regarding gender, males were predominantly involved (69.14%). This may be because the majority of HCWs at our center are males and in the Indian society, males are more habituated in smoking, drinking alcohol, outdoor activities and tendency of removal of face masks frequently. The study done by Mahajan et al<sup>9</sup> found similar results (57%). This study also shows that the disease has a predominantly urban preponderance (72.86%). The possible explanation might be that the study was conducted at a tertiary care center, which in itself is in urban area.

In the present study, comorbidities were seen in 3.42% HCWs. Among comorbidities, diabetes mellitus was observed in maximum HCWs (1.42%), followed by hypertension (0.57%), chronic respiratory illness (0.57%), ischemic heart disease (0.28%), malignancy (0.28%) and hypothyroidism (0.28%). In contrast to our study, Mahajan et al<sup>9</sup> reported 19% comorbidities in COVID-19 positive HCWs. This significant difference in comorbidities may be due to the fact that the maximum HCWs in our study were in younger age groups. They also observed that hypertension and diabetes mellitus were the most common comorbidities, which resembles the present study.

The present study shows that only 5.71% of HCWs took hydroxychloroquine drug as prophylaxis as it was advocated to have a role in the early phase of the pandemic. But, the drug did not seem much efficacious, hence, HCWs stopped taking it as prophylaxis in the later half. Therefore, majority of the HCWs did not take hydroxychloroquine as prophylaxis. Jha et al<sup>10</sup> also stated that hydroxychloroquine did not have a role in prophylaxis. Multiple systematic reviews<sup>11</sup> also concluded that there is no pertinent data to support the use of hydroxychloroquine drug outside that of research, and there is lack of clinical data to actually support its efficacy.

Among the 350 COVID-19 positive HCWs, deaths occurred in only 2 HCWs (0.57%). Mahajan et al<sup>9</sup> and Lai et al<sup>7</sup> reported similar results in their studies (1%, 0.9%). This can be explained by several reasons. In our study, most of the HCWs were young adults which accounts for better immunity. Early symptoms

were more easily noticed by HCWs which led to early diagnosis, treatment and better outcome. Also, the proper use of personal protective equipment (PPE) kits and face masks by them may be responsible for decreasing the severity of infection and death.

In the present study, out of 350 COVID-19 affected HCWs, maximum were doctors (46.29%) followed by nursing staff (37.14%), lab technicians (10.86%) and paramedical staff (5.71%). The study by Mahajan et al<sup>9</sup> showed involvement of 29% doctors, 26% nursing staff and 46% healthcare assistants and other staff. The result of the present study is contradictory to the above mentioned study. In the present study among HCWs, doctors were maximally affected (46.29%). This may be explained by the fact that doctors were the frontline warriors and were actively involved in the management of COVID-19 positive cases.

Amongst the 162 doctors affected, maximum were from Medicine department (28.40%), followed by Orthopedics (10.50%), Anesthesia (8.64%) and Internship (8.64%). The possible explanation of this higher involvement (28.40%) of doctors from Medicine department may be due to the fact that these doctors were actively and directly engaged in patient care in COVID-19 positive wards, ICU as well in severe acute respiratory illness (SARI) wards. In this pandemic, there were a lot of patients presenting with bilateral atypical pneumonias but their COVID-19 RT-PCR was repeatedly negative and they were admitted in various general medical wards, where improper use of PPE and exposure of these Medicine residents to highly suspected clinical COVID-19 patients might be one of the cause of higher involvement of doctors of this department. Orthopedicians are often involved due to operating on emergency cases of trauma without knowing the COVID-19 status of the patient. The surgeries are for longer hours and thus, increase the chances of exposure of the doctors. Anesthetists are involved in aerosol generating procedures like mechanical ventilation and noninvasive ventilation, which can lead to their increased chances of exposure. Also, Interns are primarily affected because at our center, they are doing the job of sampling of COVID-19 suspect and positive cases, which leads to increased risk for them.

## CONCLUSION

From the present study, we conclude that HCWs affected by COVID-19 are mainly young adult males from urban areas, without significant comorbidities. The outcome in COVID-19 positive HCWs is favorable

due to better immunity, awareness, prompt diagnosis and treatment. We recommend that all HCWs as well as their family members and close contacts should be regularly tested for COVID-19 as they are the most precious resource for every country. Special attention needs to be paid to protect HCWs from cross infection from other HCWs. HCWs are at higher risk of being exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and could potentially have a role in hospital transmission. Among HCWs, doctors are most prone to develop the infection, especially the ones from departments of Medicine, Orthopedics, Anesthesia and Interns.

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## Law on Euthanasia in India

Life and death as concepts have invited many thinker, philosopher, writer and physician to define or describe them. Swami Vivekananda expects one to understand that life is the lamp that is constantly burning out and further suggests that if one wants to have life, one has to die every moment for it. One may like to compare life with constant restless moment spent in fear of extinction of a valued vapour; and another may sincerely believe that it is beyond any conceivable metaphor. Death is complicated and life is a phenomenon which possibly intends to keep away from negatives that try to attack the virtue and vigour of life from any arena.

In spite of all the statements, references and utterances, be it mystical, philosophical or psychological, the fact remains, at least on the basis of conceptual majority, that people love to live - whether at eighty or eighteen - and do not, in actuality, intend to treat life like an—autumn leaf.

The perception is not always the same at every stage. There comes a phase in life when the spring of life is frozen, the rain of circulation becomes dry, the movement of body becomes motionless, the rainbow of life becomes colorless and the word life' which one calls a dance in space and time becomes still and blurred and the inevitable death comes near to hold it as an octopus gripping firmly with its tentacles, so that the person shall rise up never.

The ancient Greek Philosopher, Epicurus, has said, although in a different context:

*Why should I fear death?*

*If I am, then death is not.*

*If death is, then I am not.*

*Why should I fear that which can only exist when I do not?*

But there is a fallacy in the said proposition. It is because mere existence does not amount to presence. And sometimes, there is a feebleness of feeling of presence in semireality state when the idea of conceptual identity is lost, quality of life is sunk and the sanctity of life is destroyed and such destruction is denial of real living.

The society at large feel that a patient should be treated till he breathes his last breath.

Every doctor is supposed to take specific oath that he will make every attempt to safe the life of the patient whom he/she is treating and who is under his/her

treatment. This oath, thus, puts a moral and professional duty upon a doctor to do everything possible, till the last attempt, to save the life of a patient.

The Medical Council of India (MCI) Code of Ethics rejects Euthanasia (deliberately ending a patient's life at his/her own request or at the request of close relatives).

**“6.7 Euthanasia: Practicing euthanasia shall constitute unethical conduct.** *However, on specific occasion, the question of withdrawing supporting devices to sustain cardio-pulmonary function even after brain death, shall be decided only by a team of doctors and not merely by the treating physician alone. A team of doctors shall declare withdrawal of support system. Such team shall consist of the doctor in-charge of the patient, Chief Medical Officer/Medical Officer in-charge of the hospital and a doctor nominated by the in-charge of the hospital from the hospital staff or in accordance with the provisions of the Transplantation of Human Organ Act, 1994.”*

If that is so, would it not be against medical ethics to let a person die by withdrawing medical aid or, even for that matter, life supporting instruments.

Medical scientists have been, relentlessly and continuously, experimenting and researching to find out better tools for not only curing the disease with which human beings suffer from time to time, noble attempt is to ensure that human life is prolonged and in the process of enhancing the expectancy of life, ailments and sufferings therefrom are reduced to the minimal. There is, thus, a fervent attempt to impress the quality of life.

It is this very advancement in the medical science which creates dilemma at that juncture when, in common perception, life of a person has virtually become unlivable but the medical doctors, bound by their Hippocratic Oath and medical ethics want to still spare efforts in the hope that there may still be a chance, even if it is very remote, to bring even such a person back to life.

The Hippocratic Oath taken by a doctor and the MCI Code of Ethics may make him feel that there has been a failure on his part and sometimes also make him feel scared of various laws. There can be allegations against him for negligence or criminal culpability.

There is a distinction between the administration of lethal injection or certain medicines to cause painless

death and nonadministration of certain treatment, which can prolong the life in cases where the process of dying that has commenced is not reversible or withdrawal of the treatment that has been given to the patient because of the absolute absence of possibility of saving the life. To explicate, the first part relates to an overt act whereas the second one would come within the sphere of informed consent and authorized omission. The omission of such a nature will not invite any criminal liability if such action is guided by certain safeguards. The concept is based on nonprolongation of life where there is no cure for the state the patient is in and he, under no circumstances, would have liked to have such a degrading state.

In the landmark judgment *Common Cause versus Union of India*, 2018 (5) SCC 1, the Hon'ble Constitution Bench of 4 Judges of Supreme Court held that euthanasia is basically an intentional premature termination of another person's life either by direct intervention (active euthanasia) or by withholding life-prolonging measures and resources (passive euthanasia) either at the express or implied request of that person (voluntary euthanasia) or in the absence of such approval/consent (nonvoluntary euthanasia).

Active euthanasia also includes physician-assisted suicide, where the injection or drugs are supplied by the physician, but the act of administration is undertaken by the patient himself. Active euthanasia is not permissible in most countries.

Passive euthanasia occurs when medical practitioners do not provide life-sustaining treatment (i.e., treatment necessary to keep a patient alive) or remove patients from life-sustaining treatment. This could include disconnecting life support machines or feeding tubes or not carrying out life-saving operations or providing life-extending drugs. In such cases, the omission by the medical practitioner is not treated as the cause of death; instead, the patient is understood to have died because of his underlying condition.

Further, In *Gian Kaur versus State of Punjab*, (1996) 2 SCC 648, the Hon'ble Constitution Bench of Apex Court expounded that the word "life" in Article 21 has been construed as life with human dignity and it takes within its ambit the "right to die with dignity" being part of the "right to live with dignity". As part of the right to die with dignity in case of a dying man who

is terminally ill or in a persistent vegetative state, only passive euthanasia would come within the ambit of Article 21 and not the one which would fall within the description of active euthanasia in which positive steps are taken either by the treating physician or some other person. That is because the right to die with dignity is an intrinsic facet of Article 21.

In *Aruna Ramachandra Shanbaug versus Union of India*, 2011 (15) SCC 480, Hon'ble Supreme Court has observed that autonomy means the right to self-determination where the informed patient has a right to choose the manner of his treatment. To be autonomous the patient should be competent to make decisions and choices. In the event that he is incompetent to make choices, his wishes expressed in advance in the form of a Living Will, or the wishes of surrogates acting on his behalf ('substituted judgment') are to be respected.

Thus, all adults with the capacity to consent have the common law right to refuse medical treatment and the right of self-determination. Doctors would be bound by the choice of self-determination made by the patient who is terminally ill and undergoing a prolonged medical treatment or is surviving on life support, subject to being satisfied that the illness of the patient is incurable and there is no hope of his being cured.

In "*Common Cause versus Union of India*, 2018 (5) SCC 1, the Constitution Bench of Hon'ble Supreme Court held that Advance Medical Directive would serve as a fruitful means to facilitate the fructification of the sacrosanct right to life with dignity. The said directive will dispel many a doubt at the relevant time of need during the course of treatment of the patient. That apart, it will strengthen the mind of the treating doctors as they will be in a position to ensure, after being satisfied, that they are acting in a lawful manner. However, Advance Medical Directive cannot operate in abstraction. The Hon'ble Court in the said judgment has enumerated various safeguards and procedure of advance medical derivatives and also in cases where there is no advance medical derivatives which will remain enforced till Parliament makes a law on Advance Medical Derivatives.



## News and Views

### COVID-19 Hospitalizations 3-fold Higher in US States with Less Than Half of Residents Vaccinated

Average coronavirus disease 2019 (COVID-19) hospitalization rates seem to be around 3-fold higher in states where less than half of the residents are fully vaccinated compared to the average in the states that have vaccinated over half of their residents, revealed a CNN analysis.

Additionally, the COVID-19 case and fatality rates have been over twice as high in states that have vaccinated less than half of their residents. As per data obtained from the US Department of Health and Human Services, average current hospitalizations among states with less than half of residents vaccinated was 14.4 per 1,00,000 residents, while that in states that have vaccinated more than half of their residents stood at 4.9 per 1,00,000 residents. Daily COVID-19 case rate as per Johns Hopkins University data, was 23.7 per 1,00,000 residents in states that have vaccinated less than half of residents compared to 9.3 per 1,00,000 residents among states with more than half of residents vaccinated... (CNN, July 29, 2021)

### Some Gut Bacteria Linked to Lower Diabetes Risk

More diverse gut bacteria and higher abundance of 12 butyrate-producing bacteria have been found to be tied to less insulin resistance and less type 2 diabetes in a population-based observational study.

The study published in *JAMA Network Open* also identified several bacteria that ferment dietary fiber in the gut to produce butyrate, which may contribute to the protection against type 2 diabetes.

The study confirmed that low diversity in gut microbiome is linked with a heightened risk of obesity and type 2 diabetes. A higher abundance of each of seven types of butyrate-producing bacteria, namely *Christensenellaceae*, *Christensenellaceae R7* group, *Marvinbryantia*, *Ruminococcaceae UCG005*, *Ruminococcaceae UCG008*, *Ruminococcaceae UCG010* and *Ruminococcaceae NK4A214* group, was shown to be tied to lower insulin resistance, after adjusting for confounders like diet and drugs. Additionally, a higher abundance of each of five types of butyrate-producing bacteria, including *Clostridiaceae 1*, *Peptostreptococcaceae*, *C sensu stricto 1*, *Intestinibacter*

and *Romboutsia*, was linked with less type 2 diabetes... (Medscape)

### US FDA Agrees to Extend Shelf-life of J&J COVID-19 Vaccine, Says Company

Johnson & Johnson (J&J) has stated that the US Food and Drug Administration (FDA) extended the shelf-life of its COVID-19 vaccine from 4½ to 6 months. The decision came after the data obtained from ongoing studies indicated that the vaccine is stable at 6 months while refrigerated at 2-8°C or 36-46°F. The agency stated, in a letter to the company, that it had reviewed the data provided by J&J, and on the basis of the information provided, it agrees with the extension of the vaccine's shelf-life. The extension also applies to the vaccine batches that might have expired before the letter was issued, under the condition that they were stored at the suggested temperature, said the agency... (Reuters)

### Pfizer Third Dose Strongly Boosts Protection Against Delta Variant, Shows Data Released by Company

A third dose of the Pfizer/BioNTech vaccine against COVID-19 has the potential to strongly improve protection against the Delta variant, more than the protection provided by the standard two dose regimen, suggest latest data released by Pfizer.

The data indicate that the levels of antibodies that protect against the Delta variant increase by about 5 times in individuals aged 18 to 55 years who receive a third dose of the vaccine. Additionally, among people aged 65 to 85 years, antibody levels that protect against Delta variant rise by 11-fold more than that after the second vaccine dose.

The data have not yet been peer-reviewed and it is unclear if the improved antibody levels actually correlate to better protection... (CNN)

### Shorter Antibiotic Regimen Better in Men with UTI

Seven days of antibiotic treatment among afebrile men with suspected urinary tract infections (UTI) was found to be as effective as a 14-day regimen in a randomized, double-blind trial published in *JAMA*.

Among more than 250 men with suspected symptomatic UTI included in the as-treated analysis, 93.1% of the patients in the 7-day group had resolution of symptoms by 14 days after completing the antibiotic treatment, compared to 90.2% of the patients in the 14-day group. There was a difference of 2.9%, meeting the noninferiority criterion of 10%. A secondary as-randomized analysis conducted among more than 270 men revealed that symptom resolution was noted in 91.9% of the patients in the 7-day regimen group vs. 90.4% in the 14-day regimen group, with a difference of 1.5%... (*Medpage Today*)

### **Pfizer, AstraZeneca Vaccine Antibody Levels Start Decreasing After 6 Weeks**

The antibody levels start decreasing 6 weeks after complete inoculation with Pfizer and AstraZeneca COVID-19 vaccines, and can decrease by over 50% over 10 weeks, suggests a study published in *The Lancet*.

Investigators from University College London (UCL), UK noted that if the antibody levels continue to decline at this rate, the protective effects of the vaccines may also start to dwindle, especially against the new variants. The UCL Virus Watch study noted that antibody levels were considerably higher after two doses of the Pfizer vaccine compared to the AstraZeneca vaccine. Additionally, the levels of antibodies were higher in vaccinated individuals compared to those who had a previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection... (*ET Healthworld – PTI*)

### **US Urged Fully Vaccinated to Wear Masks Indoors in Some Places**

People of America who have been fully vaccinated against COVID-19 must start wearing masks again in indoor public places in areas where the infection is showing a rapid spread, stated US health authorities.

The US Centers for Disease Control and Prevention (CDC) also recommended that all students, teachers and staff at schools for kindergarten up to 12th grade should wear masks, irrespective of their vaccination status. COVID-19 cases have been on the rise in the country owing to the highly transmissible Delta variant, which is accountable for over 80% of the cases in the US. President Joe Biden stated that ramping up vaccination and wearing masks would help the country evade lockdowns and closure of schools... (*Reuters*)

### **Diabetes Duration Tied to Increasing Heart Failure Risk**

Longer the duration of diabetes, greater the risk for developing heart failure, stated an analysis of around 10,000 US adults followed for about 23 years. A multivariable analysis revealed that there was a steady and significant escalation in the rate of incident heart failure with increase in diabetes duration. Among 168 study subjects, constituting 2% of the total study group, who had diabetes for at least 15 years, the incidence of heart failure was shown to be around three times higher than among 4,802 individuals (49%) who never had diabetes or prediabetes, reported researchers in *JACC Heart Failure*.

Individuals with prediabetes, who constituted 32% of the study population, demonstrated a significant yet modest increase in the rate of incident heart failure - 16% higher than control group that never developed diabetes. People with diabetes for duration of 0-4.9 years, 5.0-9.9 years or 10-14.9 years, demonstrated a steady rise in relative incident heart failure rates of 29%, 97% and 210%, respectively, compared to controls... (*Medscape*)

### **Patients with Hypertension Most Likely to Develop Post-COVID Complications**

A recent analysis of medical records of more than 1,800 patients admitted to hospitals run by the Mayo Clinic in the United States has shown that patients with hypertension have the greatest odds of developing complications after COVID-19 infection.

Another study involving 18,000 COVID-19 patients conducted by Max Healthcare has also found a role of hypertension in complications. The study conducted in the US revealed that hypertension was tied to 10 complications, including acute respiratory distress syndrome, improper beating of the heart and anemia. In the analysis conducted with the help of an artificial intelligence (AI) platform developed by nference Labs, the other most significant factors that predicted complication in early COVID-19 infection included cardiovascular chronic disease, such as heart failure, coronary artery disease, cardiomyopathy and chronic kidney disease... (*ET Healthworld – TNN*)

### **COVID-19 has Considerable Impact on Intelligence in Recovered Patients, Says Study**

A severe COVID-19 infection that involves hospital admission and ventilator support can have a considerable impact on a recovered patient's intelligence



as part of long-COVID symptoms, reported a UK study. Investigators assessed 81,337 participants from January through December 2020 as part of the Great British Intelligence Test. The questionnaire items included self-report of suspected and confirmed COVID-19 infection and respiratory symptoms. The results agree with the reports of long-COVID, where brain fog, difficulty in concentrating and difficulty finding the correct words are common, stated the study. Recovered individuals had significant cognitive deficits compared to controls after controlling for age, gender, education level, racial-ethnic group, pre-existing medical disorders, tiredness, depression and anxiety, and income.

The findings are published in *The Lancet - EclinicalMedicine...* (NDTV – PTI)

### Safe to Take Second mRNA Vaccine Dose After Allergic Reaction to First

Individuals who had an allergic reaction to a first dose of the Pfizer/BioNTech or Moderna mRNA COVID-19 vaccine tolerated a second dose safely, reported a retrospective, multicenter study.

Overall, 17% of the 189 individuals with initial allergic reactions had anaphylaxis. Other reactions to the first dose included erythema, dizziness, tingling, throat tightness, hives and wheezing or shortness of breath. Among the 189 people with initial allergic reactions, researchers assessed 159 (84%) who took the second dose. All the individuals, including 19 people with first-dose anaphylaxis, tolerated the second dose. Thirty-two people who took a second dose developed immediate and potentially allergic symptoms. About 20% of the individuals had symptoms with the second dose, but they were manageable and not anaphylactic, noted researchers. The findings are published in *JAMA Internal Medicine...* (Medscape)

### A New Treatment Option for Children with Type 2 Diabetes

Exenatide extended-release has now been accorded US FDA approval for use in children aged  $\geq 10$  years with type 2 diabetes in addition to diet and exercise to improve glycemic control. This makes it the second glucagon-like peptide-1 receptor agonist approved for use in pediatric type 2 diabetes, after liraglutide, which was approved in 2019.

This injectable formulation is not recommended as a first treatment option for patients whose disease is not adequately controlled through diet and exercise. It is not to be used for children with type 1 diabetes.

Exenatide extended-release has earlier been approved to treat adults with type 2 diabetes.

A boxed warning has been added to prescribing information about the increased risk of thyroid C-cell tumors. The FDA has cautioned that patients with family history of medullary thyroid carcinoma, patients with multiple endocrine neoplasia syndrome type 2 or a history of drug-induced immune mediated thrombocytopenia or those with previous hypersensitivity to exenatide or any of its components should avoid the therapy.

While the overall side effects reported (injection site reactions, headaches and gastrointestinal discomfort) were similar to those seen in adults, warnings about hypoglycemia when used with insulin or insulin secretagogues, acute kidney injury, gastrointestinal disease, immunogenicity, allergic reactions (such as anaphylaxis and angioedema) and drug-induced immune-mediated thrombocytopenia have been included. Type 2 diabetes mellitus was earlier perceived as adult-onset diabetes. But, its prevalence in children and adolescents has increased in recent years. Therefore, it is important to screen children at high risk such as positive family history of type 2 diabetes mellitus and/or clinical features of insulin resistance (such as hypertension, dyslipidemia, polycystic ovarian syndrome or acanthosis nigricans). Type 2 diabetes mellitus is emerging as a new clinical problem within pediatric practice. Recent reports indicate an increasing prevalence of type 2 diabetes mellitus in children and adolescents around the world in all ethnicities, even if the prevalence of obesity is not rising. Therefore, a screening seems meaningful especially in high risk groups such as children and adolescents with obesity, relatives with type 2 diabetes mellitus, and clinical features of insulin resistance (hypertension, dyslipidemia, polycystic ovarian syndrome or acanthosis nigricans).

The American Diabetes Association (ADA) Standards of Medical Care in Diabetes—2021 recommends risk-based screening for prediabetes and/type 2 diabetes after the onset of puberty or after 10 years of age, whichever occurs earlier, in children and adolescents with overweight (body mass index [BMI]  $\geq 85$ th percentile) or obesity (BMI  $\geq 95$ th percentile) and who have one or more risk factor for diabetes.

Metformin is the only oral antidiabetic drug approved for use in children with type 2 diabetes, while the approved injectables include insulin, liraglutide and now exenatide.

(Source: FDA OKs extended-release exenatide for children with type 2 diabetes - Medscape - Jul 23, 2021; <https://content.gooddelivery.com/accounts/USFDA/bulletins/2e98d66>; ADA Standards of Medical Care 2021)

### France Approves Bill to Handle Fourth Wave of COVID-19

French lawmakers have approved a bill recently which will mandate COVID-19 vaccinations for healthcare workers and require a health pass in several social venues as the country fights the fourth wave of COVID infections.

People visiting museums, cinemas or swimming pools are already denied access if they fail to show a pass that confirms that they have been vaccinated against COVID-19 or have had a recent negative test. The pass has been needed for large-scale festivals or for clubbing. From August, the pass will be required to access restaurants and bars and for long-distance travel by train and plane as well. These measures will end on November 15. A final approval from the constitutional court is needed for the law to come into effect... (Reuters)

### Low-income Countries Acquired Only 0.27% of COVID Vaccine Doses Administered Thus Far

Low-income countries have received a mere 0.27% of the COVID-19 vaccine doses administered globally thus far, while high-income countries and upper-middle-income countries have received over 80% of the doses.

Among the 27 low-income countries, 23 are in Africa. Owing to the wide inequality in vaccine distribution, out of the 52 African countries, 38 have been able to administer at least one dose of a COVID vaccine to less than 5% of the population. Several countries in Africa have also recorded a recent rise in COVID-19 infections, mostly accountable to the highly contagious Delta variant. Around 27% of the global population has been administered at least one vaccine dose, while in Africa, only 3.13% of the population has received at least one dose... (The Hindu)

### Flu Activity During the Pandemic: CDC Report

The circulation of influenza and several other respiratory viruses diminished during the pandemic in 2020; however, it was found to increase during the spring of 2021, noted researchers. Flu activity was shown to reduce in March 2020, and continued to remain low until May 2021, as <0.4% of respiratory samples tested positive for influenza per week of the

flu season. The patterns were similar for several other respiratory pathogens, including respiratory syncytial virus, parainfluenza viruses, and common human coronaviruses, reported researchers in *Morbidity and Mortality Weekly Report*. Human metapneumovirus and respiratory adenovirus were found to be circulating at low levels from 2020 to 2021. Rhinovirus and enterovirus were low till May 2020 before they rose to near pre-pandemic levels. Experts had warned of a COVID and flu 'twindemic' in the fall of 2020. However, from October 2020 to May 2021, circulating influenza had the lowest activity since 1997... (Medpage Today)

### EMA Approves Moderna Vaccine for 12 to 17 Years Age Group

The European medicines regulator has granted approval for the use of Moderna COVID-19 vaccine in children aged 12 to 17 years. This is the second vaccine that has been approved for use in adolescents in Europe. The European Medicines Agency (EMA) announced that the use of the Moderna vaccine, named Spikevax, in children aged between 12 and 17 years, will be the same as in individuals 18 years of age and above. Two shots will be given at an interval of 4 weeks. The Pfizer/BioNTech vaccine was approved for youngsters in Europe in May.

The agency stated that the Moderna vaccine was evaluated in 3,732 children aged 12 to 17 years. The vaccine led to a comparable antibody response in 12- to 17-year-old age group as that noted in young adults, 18 to 25 years of age... (NDTV - AFP)

### Countries Promote Mix-and-Match COVID Vaccines

Despite preliminary data, certain countries are going ahead with mixing and matching mRNA and adenoviral vector COVID-19 vaccines, usually guided by supply constraints. Germany has made an official recommendation to mix-and-match vaccines, encouraging people to get a dose of an mRNA vaccine after their AstraZeneca jab. Chancellor Angela Merkel had followed her initial AstraZeneca shot with a Moderna jab in June. Canada and Thailand have also started administering COVID-19 shots on a heterologous schedule. While the EMA and the European Centre for Disease Prevention and Control (ECDC) did not issue any specific recommendation, but they promoted mix-and-match approach in a press release which stated that good scientific grounds exist to expect that this approach would be safe and effective when used in vaccination against COVID-19... (Medpage Today, July 22, 2021)

# The Spiritual Heart: Your Heart and My Heart are One

“*Tat tvam asi*” is a mahavakya in the ancient Sanskrit texts of the Upanishads. It translates as “I am that” and means “You and I are same” or “your heart and my heart are one”.

Whenever we point to our own self, we put our hand on our heart; we also put our hand on our heart when we say “I love you from the bottom of my heart”.

Does the consciousness reside in the celiac plexus (Manipura chakra) or thymus plexus (Anahata chakra)? We do not know. Manipura chakra is associated with fire and the power of transformation. The Anahata chakra manifests unconditional love, forgiveness and patience.

Our ancient scriptures and the Bible say that the heart is the size of a thumb and it is in the heart that our consciousness (soul) resides.

- **In Svetasvatara Upanishad (5.8, 5.9):** “Soul is the size of a thumb, bright as the sun, when coupled with conception and ego. But with only the qualities of understanding and soul, it appears the size of the point of an awl. This life is the hundredth part of the point of a hair divided a hundred times, and yet in it is infinity”. Here the sruti is speaking metaphorically, because actually the soul is atomic in size. Therefore in the next verse (Svet. U. 5.9) the soul is compared to a fraction of the tip of a hair. These comparisons are meant to indicate that the individual soul is atomic rather than all-pervasive.
- According to **Vedanta Sutra**, the idea that God resides in the physical heart the size of the thumb is for the sake of conceptualization during meditation, and is thus a metaphorical description. The size of the thumb refers to the size of the human heart. God is in reality all pervading and atomic at the same time.
- **Atharva Veda:** The soul is a particle of God.
- **Jain metaphysicists** refer to it as of varying sizes, small in a child, big in adults and old people and very big in elephants.
- **Nemi Chandra in Dravya Sangrah-2:** Soul is characterized by knowledge and vision, has the same extent as its own gross body.
- **Katha Upanishad (1.2.20):** Spirit, the size of a thumb “angush matra”, is the inner soul, always seated in the heart of creatures.
- **Katha Upanishad Part Fourth XII:** The Purusha (Self), of the size of a thumb, resides in the middle of the body as the lord of the past and the future, (he who knows Him) fears no more. This verily is That. The seat of the Purusha is said to be the heart, hence it “resides in the middle of the body.” Although it is limitless and all-pervading, yet in relation to its abiding-place. It is represented as limited in extension, “the size of a thumb”. This refers really to the heart, which in shape may be likened to a thumb. Light is everywhere, yet we see it focused in a lamp and believe it to be there only; similarly, although the life-current flows everywhere in the body, the heart is regarded as peculiarly its seat.
- **Garuda Puran:** Ultimately, the soul, which is not more than the size of a thumb, reluctantly comes out from the body as the attachment with the world exists even after his.
- **Gaudiya Acharya Sri Baladeva Vidyabhusana** in his Govinda Bhasya commentary on the Vedanta Sutra (1.2.7, 1.3.24-25.): During meditation Paramatma does appear to the yogi or devotee as a localized form in his heart, but in general Paramatma is all-pervasive and all-knowing.
- **Unknown:** According to some Vedic scholars the soul enters the human form like 4-8 weeks after conception, like when the fetus is the size of a thumb.
- **Bhagavad Gita 15.15:** “I (soul) am seated in everyone’s heart, and from Me come remembrance, knowledge and forgetfulness. By all the Vedas, I am to be known. Indeed, I am the compiler of Vedanta, and I am the knower of the Vedas.”
- **Vedanta Sutra II, 6, 17:** The person of the size of a

thumb, the inner Self, is always settled in the heart of men. Let a man draw that Self forth from his body with steadiness, as one draws the pith from a reed. Let him know that Self as the Bright, as the Immortal.

- **Swami Muktananda, Play of Consciousness, p. 85:** "The whole body is like a lotus which has four petals of four kinds, colors and sizes....The first is the gross body, its color is red. The second petal is

the subtle body, in which we sleep and experience dreams. It is the size of a thumb, and its color is white. The third petal is the causal body. It is the size of the tip of third finger, and its color is black. The fourth petal is the supra-causal body, which is as small as a sesame seed. Its color is blue.... It is very brilliant; it is the foundation of sadhana; it is the highest inner vision."

- **Matthew 5; 8:** Soul resided in the heart: "Blessed are the pure in heart, for they shall see God."



# *The Asian Journal of* **DIABETOLOGY** Information for Authors

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

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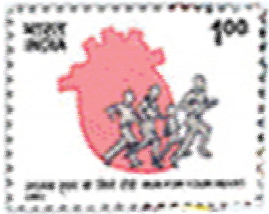
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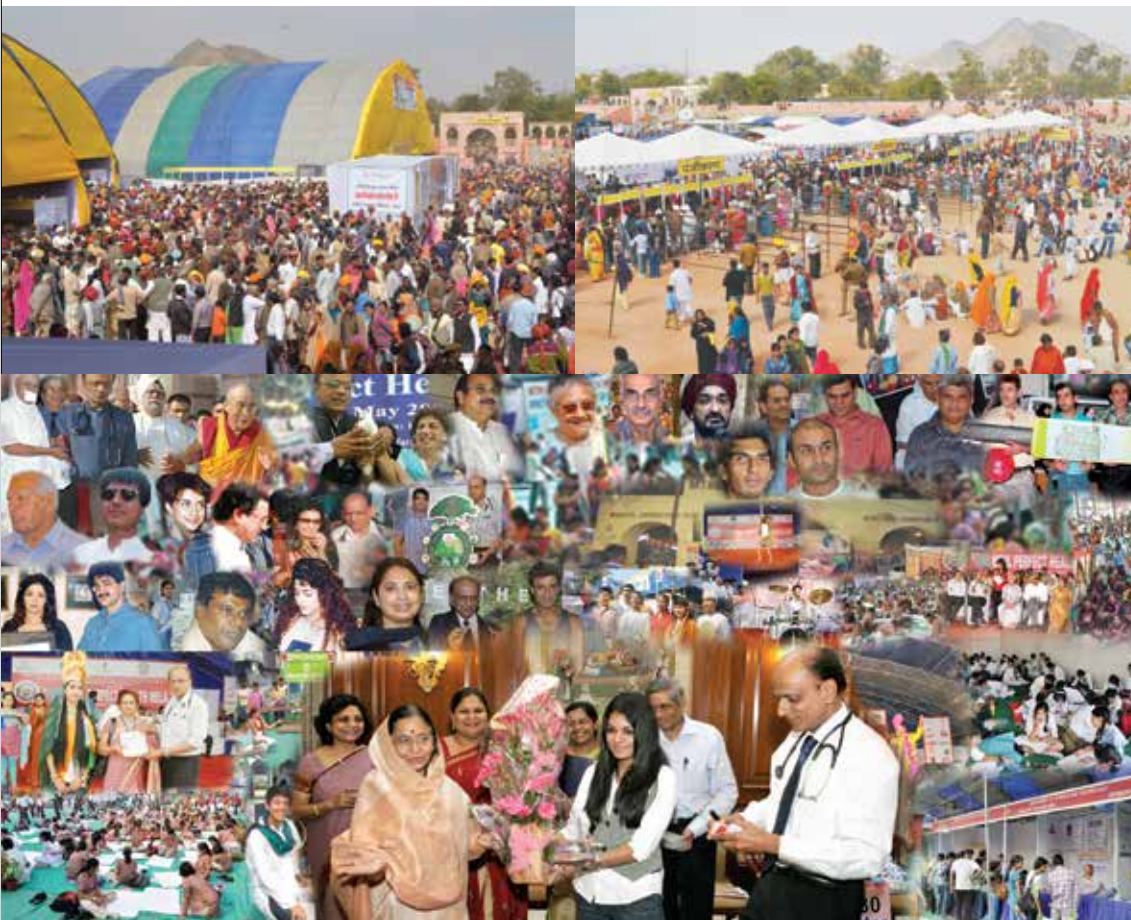
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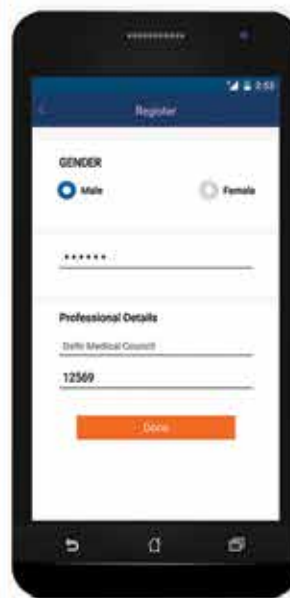
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