



Prevalence of loss of appetite in patients visiting primary care physicians: A Cross-sectional Survey

S Banerjee¹, M Vijayamohan², AC Patel³, SB Singh⁴, PV Manjrekar⁵, R T Rathod⁵
SPLASH Study Investigators*

Abstract

Background and Objective: Loss of appetite (LOA) during illness impacts individual well-being and quality of life. An epidemiological survey was conducted on the prevalence of LOA.

Methodology: Multi-centre, non-interventional, cross-sectional, survey of LOA in Indian participants recuperating from various health disorders.

Results: A total of 15914 participants were enrolled into the study. Of the 15914 participants enrolled, 63.5% were men and 36.5% were women, with a mean age of 38.5 years and majority of participants (68.7%) had infectious diseases. Of which, 80.3% participants were reported with infections and infestations disorders as the most frequent infectious condition. The prevalence of LOA was 93.1% (95% CI: 92.7%, 93.5%) with 33.8% participants having mild, 47.7% had moderate and 11.6% had severe to very severe LOA problem. The prevalence of fatigue was 91.1% (95% CI, 90.5, 91.4) of which, 44.4% had mild, 36.8% had moderate, and 9.8% had severe to very severe fatigue. LOA and fatigue was highest in participants with infections and infestations (93.8% and 91.7% respectively), with typhoid being the most common cause. The risk of LOA was 1.5 times more in participants with a past history of any medical condition and 1.31 times more in subjects with infectious diseases ($p < 0.0001$). The risk of fatigue was 1.19 times more in participants aged > 40 years and 1.27 times more in participants with family history of any medical condition ($p < 0.0001$).

Conclusions: The survey observed that about 93% and 91.1% of Indian participants with various health conditions suffered from LOA and fatigue respectively. Infectious disease especially typhoid was the commonest cause of LOA and fatigue. This is the first study documenting the extent of the problem in pan-Indian participants.

Keywords: Fatigue-Health disorders-India-Infections and infestations-Loss of appetite- Typhoid.

Introduction

Appetite is the internal driving force for the search, choice and ingestion of food [1]. Subjective sensation of hunger, satiety, other appetite sensations and desire to eat specific type of food may be influenced by a number of different internal factors including physiological and psychological [2]. Lack of appetite (LOA) and loss of well-being is a major concern for patients and their families.

Food intake is integrated with appetite loss or factors causing appetite loss, cognitive impairment [3], vomiting, stomatitis, dysphagia, dietary restrictions etc. [4]. Any fever may also cause a temporary LOA. A prolonged fever may affect appetite to cause weight loss. Disease may not only dampen the appetite but LOA may further lead to deficiency of nutrients, and affect quality of life. LOA can also be perceived as an indicator of both quality of life and severity of disease in cancer patients, and is independently linked to survival [5] and correlates significantly with physical function [6].

Fatigue is a complex symptom comprising a set of complaints including lethargy, malaise, lassitude and exhaustion and can be defined as a subjective perception and/or experience related to disease, emotional state and/or treatment [7,8]. Because of difficulties in

defining and treating fatigue, it is often overlooked by physicians caring for patients with hepatic and other various disorders [9]. Studies on LOA and fatigue during various clinical conditions including prolonged fever, postoperative cases and acute or chronic illness are lacking in India. The objective of the present epidemiological survey [SPLASH: Survey of Prevalence of Loss of Appetite in Subject with Health Disorders] was to find out the prevalence of LOA and fatigue during various health disorders in India. We believe that the outcome of this survey will help us to highlight the extent of LOA and fatigue in various health disorders and the need for strategies to improve appetite and replenishment of nutrients during ill-health and convalescence and aid in a healthy recovery.

Materials and Methods

Study designing & setting: The present study was a cross-sectional, multi-centric survey carried out between Jan 2013 to Dec 2014, in participants suffering from various health disorders visiting primary healthcare

¹Consultant Physician & Diabetologist, Apollo Clinic, Bardhaman, India.

²Civil Surgeon, Osmania Medical College and General Hospital, Hyderabad, India.

³Consultant Physician, Usha Clinic, Mumbai

⁴Consultant Physician, Narain Clinic, Varanasi, India

⁵Bayer Zydus Pharma Pvt. Ltd, Thane, India

* Splash Investigators List attached at the end of manuscript

Address of Correspondence

Dr Pravin V Manjrekar
Bayer Zydus Pharma Pvt Ltd, Medical Affairs – R&D,
5th Floor, New Bayer House, Central Avenue, Hiranandani
Estate, Thane West - 400 607, India.
Email: pravin.manjrekar@bayerzyduspharma.com

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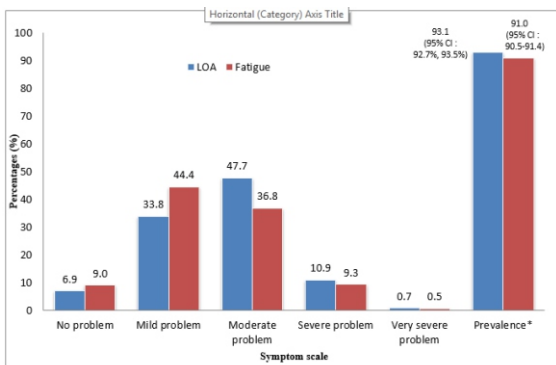


Figure 1 - Distribution and prevalence of LOA and Fatigue Assessment

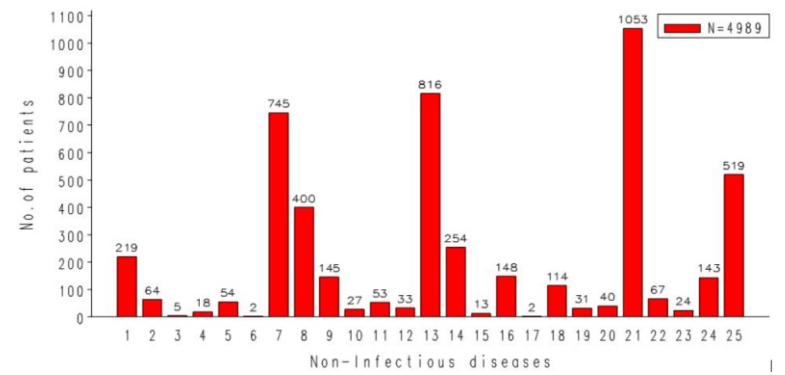


Figure 2 - Distribution of Non-Infectious Diseases

1. Blood and lymphatic system disorders
2. Cardiac disorders
3. Congenital, familial and genetic disorders
4. Ear and labyrinth disorders
5. Endocrine disorders
6. Eye disorders
7. Gastrointestinal disorders
8. General disorders and administration site conditions
9. Hepatobiliary disorders
10. Immune system disorders
11. Injury, poisoning and procedural complications
12. Investigations
13. Metabolism and nutrition disorders
14. Musculoskeletal and connective tissue disorders
15. Neoplasms benign, malignant and unspecified (Incl Cysts and Polyps)
16. Nervous system disorders
17. Pregnancy, puerperium and perinatal conditions
18. Psychiatric disorders
19. Renal and urinary disorders
20. Reproductive system and breast disorders
21. Respiratory, thoracic and mediastinal disorders
22. Skin and subcutaneous tissue disorders
23. Social circumstances
24. Surgical and medical procedures
25. Vascular disorders.

physicians at 258 centres across the country. Willing participants were examined by the investigators and all observations were recorded in the case record form (CRF). Inclusion criteria for the participants were as follows: i) Men and non-pregnant women ≥18 years of age recuperating from healthcare disorders like: malaria fever, typhoid or enteric fever, hepatitis ii) acute infections including respiratory, urinary tract infections etc. treated with antibiotics iii) patients discharged from hospital after general surgical procedures like acute appendectomy etc. and iv) patients having any other condition. Patients unwilling to provide informed consent and comply with the study procedure and patients using

drugs which affect appetite were excluded from the study. The study was carried out after obtaining a written informed consent from the participants and approval by the local ethics committee or Institutional Review Board. The study was registered at ClinicalTrials.gov Identifier: NCT01592149 and CTRI No- CTRI/2013/01/003327. The primary objective of the study was to assess the prevalence of LOA in Indian participants recouping from various health

disorders. The secondary objective was to assess the prevalence and severity of fatigue in the study population. Primary outcome variables include percentage of participants with LOA and distribution of LOA with respect to disease. The secondary outcome variables were percentage of participants with fatigue, distribution of fatigue among the participants with respect to disease and percentage of participants with moderate to very severe fatigue. The severity of LOA and

Table I - Summary of Demographic Characters

Variable	Statistics/Category	(N=15914)
Age (Years)*	n	15914
	Mean (SD)	38.5 (11.41)
	Median	36
	Q1, Q3	30.0, 45.0
	Min, Max	18, 101
Sex	Male	10107 (63.5%)
	Female	5807 (36.5%)
	Total	15914 (100.0%)
Race	White	436 (2.7%)
	Black	280 (1.8%)
	Asian	15123 (95.0%)
	Not reported	75 (0.5%)
	Total	15914 (100.0%)

SD=Standard deviation, Q1=First quartile, Q3=Third quartile, Min=Minimum, Max=Maximum *Age (years) = ((Date of visit-Date of Birth) +1)/365.25 And for partial dates Age (years) = Year of visit-Year of Birth +1

Table II - Summary of Top 5 Medical and Family History conditions

System Organ Class	Medical History	Family History
	Number (%)	Number (%)
	(N=15914)	(N=15914)
Total no. of subjects had history of medical conditions*	3313 (20.82)	2915(18.3)
Vascular Disorders	1191 (35.95)	1348(46.2)
Metabolism And Nutrition Disorders	962 (29.04)	361(12.4)
Infections And Infestations	432 (13.04)	120(4.1)
Respiratory, Thoracic And Mediastinal Disorders	246 (7.43)	203(7.0)
Gastrointestinal Disorders	187 (5.64)	NA
Social Circumstances	NA	821(28.2)

*Denominator of % calculation = Total no. of subjects in the study. Denominator of % calculation = Total no. of subjects had history of medical conditions. Denominator of % calculation = Total no. of subjects had family history of medical conditions. NA= Not Applicable.

Table III - Summary of Top 5 Infectious Diseases

Infectious diseases - System Organ Class	(N=15914) Number (%)
Total no. of subjects had Infectious Diseases*	10925 (68.7)
Infections And Infestations	8769 (80.3)
General Disorders And Administration Site Conditions	1436 (13.1)
Gastrointestinal Disorders	392 (3.6)
Respiratory, Thoracic And Mediastinal Disorders	198 (1.8)
Hepatobiliary Disorders	93 (0.9)

*Denominator of % calculation = Total no. of subjects in the study.
Denominator of % calculation = Total no. of subjects had Infectious Diseases.

fatigue were evaluated using non-pain symptom scale, as described earlier [10]. The symptoms were rated from 1 to 5 depending on the perceived severity by the patient with 1 indicating no problem and 5 as very severe problem. The score of 2-5 (mild to very severe problem) combined was used to estimate the prevalence.

Sample size calculation: The sample size calculation was based on the prevalence of LOA and on the expected proportion of patients with LOA, approx. 38%; required precision of estimate taken as 0.72%; required confidence level taken as 95%. With the assumptions above, a sample size of 17459 patients was required to have 95% confidence so that the proportion of LOA is between 37.28% and 38.72% (38±0.72%).

Data collection and processing: Patients who agreed to participate were examined by the investigators and all observations were recorded in individually numbered CRFs. Data from the CRF was entered in the study database and validated through double data entry. Data management and statistical analysis plans were developed before the database lock.

Data analysis: For Primary and Secondary objectives analyses, descriptive statistics were provided for continuous variables with number (N) of non missing observations, mean, standard deviation (SD), median, minimum and maximum and for categorical data, descriptive statistics were presented with number (N or n) and their percentages. Proportions of above primary and secondary endpoints were presented with 95% confidence intervals. Trend Chi-square was used to analyze the trend between LOA and fatigue assessments. Kendall rank correlation was

Table IV. Multivariate Logistic Regression Analysis of LOA with respect to the risk factors

Independent variable	Category	Regression Coefficient	Standard Error of Coefficient	p-value [^]	Odds Ratio (95% CI)
Medical History	No				1.00
	Yes	0.4063	0.095	<0.0001	1.50 (1.25, 1.81)
Family History	No				1.00
	Yes	0.4955	0.1057	<0.0001	1.64 (1.33, 2.02)
Disease type	Non-Infectious				1.00
	Infectious	0.2732	0.0684	<0.0001	1.31 (1.15, 1.50)

[^]Wald Chi-square test was used to calculate the p-value

Method of regression was forward stepwise addition method.

OR=1.00 represents reference category.

Dependent variable: LOA assessment (Coded as 0-No problem; 1- Mild problem or Moderate problem or Severe problem or Very severe problem)

Other Independent variables considered were age (>40, >40), gender (Female, Male) and duration of disease-Duration of recovery/Duration of ongoing- (>6 months, > 6 months). None of these variables were statistically significant (P>0.05)

BMI was not considered for analysis due to large number of missing observations

Note: All subjects were considered for analysis

used to measure the strength of association between LOA and fatigue assessment. The hypothesis test was performed at 5% level of significance and the p value ≤ 0.05 was considered as significant.

Results

Participants and demographic data: Overall, 15914 (95.8 %) participants recovering from various health disorders were enrolled out of the 16607 subjects screened. This includes 10107 males and 5807 females with a mean (SD) age of 38.5 (11.41) years. The demographic characteristics of participants are summarized in Table I.

Medical and Family History

A total of 3313 (20.82%) participants reported a history of any medical condition. The most frequent medical history reported was vascular disorders followed by metabolic and nutritional disorders, infections and infestations, respiratory, thoracic or mediastinal disorders and gastrointestinal disorders (Table II). A total of 2915 participants had a family history of any medical condition. The most frequent family history reported was the vascular disorders followed by social circumstances which include family history of diabetes for 816 participants, metabolism and nutritional disorders, respiratory, thoracic or mediastinal

disorders and infections and infestations. A summary of top 5 medical and family history conditions is provided in Table II.

Distribution of Medical Disorders

Out of a total of 15914 participants, 10925 (68.7%) participants were classified as having infectious disorders. The breakup of various conditions included under this disorder is shown in Table III. The most frequent infectious conditions were infections such as typhoid, malaria, urinary tract, respiratory tract, tuberculosis, dysentery etc, followed by general disorders and administration site conditions, gastrointestinal disorders, respiratory thoracic or mediastinal disorders and hepatobiliary disorders. The remaining patients with non-infectious disorders included respiratory, thoracic and mediastinal disorders, followed by metabolism and nutrition disorders, gastrointestinal disorders, vascular disorders, general disorders and administration site conditions, musculoskeletal and connective tissue disorders, blood and lymphatic system disorders, nervous system disorders, hepatobiliary disorders, surgical and medical procedures, psychiatric disorders, skin and subcutaneous tissue disorders, cardiac disorders, endocrine disorders, injury, poisoning and procedural complications, reproductive system and

breast disorders, investigations, renal and urinary disorders, immune system disorders, social circumstances, ear and labyrinth disorders, neoplasms benign, congenital, familial and genetic disorders, eye disorders and pregnancy, puerperium and perinatal conditions as shown in Figure II.

Drug Treatment

A total of 8050 (50.58%) had reported the use of drug treatment. The most frequent drugs used were systemic antibacterials (n=3886; 48.27%) followed by analgesics (n= 3154; 39.18%), drugs for acid related disorders (n= 970; 12.05%), vitamins (n=725; 9.01%), appetite stimulants (n=663; 8.24%), antiprotozoals (n= 627; 7.79%), cough and cold preparations (n=466; 5.79%) and drugs for obstructive airway diseases reported for 421 (5.23%) participants.

Outcome data

Primary outcome variables

Prevalence of LOA: The prevalence of LOA was 93.1% (95% CI: 92.7% to 93.5%) in the enrolled participants. Participants with no LOA problem, mild, moderate, severe and very severe LOA problem were summarized in Figure I.

Distribution of LOA assessment with respect to medical disorders: The prevalence of LOA for the participants with medical disorder of infections and infestations was 94.40% (95% CI: 93.9% to 94.9%). In the 1836 participants reporting the medical disorder as general disorders and administration site conditions the prevalence of LOA was 92.6% (95% CI: 91.3% to 93.7%). Of the 1137 participants who reported with gastrointestinal disorders, the prevalence of LOA was 93.5% (95% CI: 91.9% to 94.9%).

Multivariate Logistic Regression Analysis of LOA with respect to the Risk factor:

Medical history, family history of medical condition and disease type showed statistically significant relationship (p value <0.0001) with LOA. Multivariate logistic regression analysis of LOA with respect to the risk factors is given in Table IV.

Secondary outcome variables

Prevalence of Fatigue: The prevalence of fatigue was 91.0% (95% CI: 90.5% to 91.4%) in the enrolled participants. A summary and analysis of fatigue assessment

and severity is provided in Table I. Distribution of fatigue assessment with respect to medical disorders: The prevalence of fatigue for the participants who were grouped as medical disorder of infections and infestations was 92.3% (95% CI: 91.7% to 92.8%), for participants with general disorders and administration site conditions the incidence of fatigue was 88.6% (95% CI: 87.1% to 90.0%) and in patients with gastrointestinal disorders it was 93.8% (95% CI: 92.2% to 95.1%).

Discussion

LOA can occur as a symptom in health disorders like cancer, metabolic disorders, infectious conditions, as a side effect of treatment [11,12]. A brief period of LOA may accompany acute illnesses. However, prolonged LOA may occur in people with a serious underlying disorder such as cancer, AIDS, chronic lung disease, and severe heart, kidney, or liver failure [13]. Prolonged anorexia can compromise host defense, and delays recovery from infection. Therefore, chronic LOA can be considered as an indicator of the presence of the disease [14,15]. A survey of 363 hospitalized patients in Spain reported that 60% of the patients ate less than the usual amount of food consumed within the last week and the most frequent reason being decreased appetite [16]. Malnutrition and infection interact with each other synergistically. Recurrent infections lead to a loss of body nitrogen and worsen nutritional status; the resulting malnutrition, in its turn, produces a greater susceptibility to infection. There is a negative nitrogen balance during infection the extent of which varies with the type and duration of infection. It has been suggested that the protein loss occurs from the body due to the catabolism induced by infection, and this loss should be made good through the provision of additional protein intake particularly during recovery. However anorexia and loss of appetite may limit this [17]. Fatigue is a multidimensional symptom involving physical, emotional, social and spiritual well-being and affecting quality of life [7]. It is one of the most common symptoms in advanced cancer and is nearly universal in the terminal stages of illness [18]. Fatigue is reported from 36% to 78% in studies of cancer patients at various stages of their disease [19]. There is a paucity of data from India and to our

knowledge, this is the first survey to assess LOA and fatigue in Indian participants. The present cross-sectional study shows that more than 75% of the participants recouping from various health disorders had mild to moderate LOA and/or fatigue problem. The survey observed that about 93.1% and 91.1% of the participants had LOA and fatigue respectively. The prevalence of LOA and fatigue was high in participants with infections and infestations (94.40% and 91.1%, respectively), typhoid being the commonest cause.

Earlier studies carried out in developing countries had shown similar prevalence of LOA in patients with typhoid [20-23]. Other studies [24,25], indicated the prevalence of anorexia during enteric fever to be 30% to 57%. Anorexia was also reported in approximately 65% of patients reported with acute hepatitis A in Seoul and Gyeonggi provinces of Korea [26]. A cross-sectional analysis of symptom in adults with influenza and other acute respiratory illness in an outpatient setting reported fatigue in 91% of the patients [27].

The wide difference in incidences of LOA and fatigue observed between various studies and the present study could be a reflection of the methodology used to collect the information.

In the present study, medical history, family history of medical condition and disease type showed statistically significant relationship (p value <0.0001) with LOA. The risk of getting LOA was 1.50 times more in participants who had medical history, 1.64 times more in participants who had family history of medical condition and 1.31 times more in participants who had infectious diseases. None of the other independent variables were found to be significant risk factors for LOA.

Age and family history showed statistically significant relationship (p value <0.0001) with fatigue. The risk of getting fatigue was 1.19 times more in participants with age >40 years and 1.27 times more in participants who had family history of any medical condition.

The current study results showed a significant positive correlation (p value <0.0001) between LOA and fatigue assessment. Trend Chi-square analysis showed that there was a significant trend across various categories of LOA and fatigue (p value <0.0001). In addition Kendall rank correlation (r) was also used

to estimate the strength of correlation between LOA and fatigue assessment. The estimated Kendall rank correlation (r) was 0.41 (95% CI: 0.40-0.42), and showed a significant positive correlation (p value <0.0001) between LOA and fatigue assessment.

The authors acknowledge the limitations of this study, and several issues must be considered while interpreting the results of the study. This study was a cross sectional study with no follow ups and was carried out on a heterogeneous population.

In conclusion the findings of the survey substantiate the fact that LOA and fatigue are frequent in various health disorders in the Indian population. LOA especially during the recovery phase as evident in the study population could prolong recovery. Hence it may be relevant to include strategies for adequate nutrition, including management of LOA and fatigue in addition to disease management to help expedite recovery.

*SPLASH Study Investigators

A Dhanalakshmi, Sathyamangalam; AK Tirkey, Raigarh; AK Gupta, Lucknow; AVV Satyanarayana, Hyderabad; Agarwal Atul Kumar, Durg; Agarwal Satish Chandra, Jhansi; Aghao Sudhir Bhaskar Rao, Nagpur; Agrawal Ashok Kumar, Gorakhpur; Aldar Dibyendu H, Kolkata; Aneerjee Sumit B, Sreerampur; Ansari Tanveer Alam, Kolkata; Arora Dharam Veer, Jalandar; Ashish Eklahare, Mumbai; Asis Maitra, Naihati; B Shashidhar, Hyderabad; BL Rusia, Jabalpur; BP Singh, Jaunpur; BV Pradeep, Bangalore; Bajpai Ashutosh, Kanpur; Banerjee BN, Ranchi; Bandhopadhyay Sumit, Siliguri; Barai Viren, Ahmedabad; Barari Kiran, Nashik; Bera Nirmal Kumar, Siliguri; Bhattacharya Sandeep, Lucknow; Bhoite Suresh Dadu, Thane; Biswas Dibjyoti, West Bengal; Biswas Jayanta, Nabogram; Bodepudi Hanumaiah, Vijayawada; Bomb Bhopal Singh, Udaipur; Borkar Amod J, Goa; Ch Nagabhushana Rao, Kurnool; Chakraborty Sunil Chandra, Bagdogra; Chandrashekhar, Tumkur; Chary Vignana, Karimnagar; Chattopadhyay Debasis, Parganas; Chaudhary Dilip, Bankura; Chaudhary Kavindra Kumar, Bihar; Choudhary Prithvi Singh, Jodhpur; Choukhar Nitin, Pune; D Rani, Coimbatore; D Anil Avha, Mumbai; DK Gupta, Delhi; DK Shivakumar, Chennai; Das Alok, Rupnaryanpur; Das Animesh, Garia; Das Kushal, Gulaghat; Das Shreeekanta, Balasore; Das Susanta, Kolkata; De Asis Kumar, Kalna; De Asis Kumar, Kalna; Debnath Tanmoy, Jalpaiguri; Deka Basanta KR, Nalbari; Desai Girish, Surat; Dey Pradip, Kaliganj; Dhir Dinesh, Firozpur; Dutta Anabil, Chakdighi; Dwivedy Ramesh

Chandra, Kalinagar; EK Ajitkumar, Mumbai; FA Qureshi, Hyderabad; Farooqui Jawad, Hyderabad; G Prakash Rao, Srikakulam; G Dayanand, Bangalore; Gaikwad Rajesh B, Mumbai; Ghosh Chittaranjan, Suri; Ghosh Rudra Pratap, Ranchi; Gogoi Arun Chandra, Dibrugarh; Gogoi Kamal Chandra, Doloka; Gogoi Mintu KR, Assam; Gohel Kalpesh, Anand; Gupta Ajit Kumar, Kolkata; Gupta Ravindra, Mumbai; HD Ashwath Narayan, Bhadravathi; Haldar Subrata, Coochbehar; Hokray Anand B, Warangal; Ingale Nagesh Sarjero, Satara; Ishteyaq Ahmed, Kolkata; J Ravikumar, Hanumakonda; J Anbalagan, Chennai; J P Sinha, Asansol; Jain Pradeep, Balod; Jaiswal Pradeep, Ahmednagar; Jambu Jain, Guna; Jha Ramesh Kumar, Darbhanga; John Joshy, Calicut; Johnson Anthony Joseph, Chennai; Joshi Mayuresh, Mumbai; Joshi Urvi P, Jalgaon; K Anand M, Thrissur; KMN Srinivas, Mancherla; K Thirupal Reddy, Kurnool; KA Venkatachalam, Chennai; KD Tibrewala, Ahmedabad; KK Bose, Durgapur; KK Srivastava, Varanasi; K Venkat Rao, Hyderabad; Kakati Ramen Kumar, Tamalpur; Kalita Pinaki Raj, Tezpur; Kantilal Pujara Nishant, Bhuj; Kapoor Kailash, Delhi; Kar Goutam, Karnataka; Katakam Narendar, Warangal; Kausar Madiha, Purnia; Kewalramani Rajesh Mohan, Mumbai; Khaja Naseerudin, Karnataka; Kulkarni Gururaj, Gulbarga; M Mahesh, Mysore; M Raja Reddy, Palakollu; MVV Prasad Rao, Tanuku; M Visweswara Rao, Secunderabad; M Rajeshwariaiah, Jammikunta; M Vijayamohan, Hyderabad; MG Manoz, Srikakulam; M Ganesan, Chennai; M Kalarimathi, Chennai; MM Dhawan, Bareilly; MP Khatri, Sumerpur; Madan Prasad, Patna; Madhusudan Reddy, Warangal; Makadia Ashish B, Bhuj; Makkar Praveen, Sriganganagar; Malhotra Ravindra K, Jammu; Manzar Abubakar Zeeshan, Kerala; Maurya Sanjeev Kumar, U.P.; Mishra Sanjay Kumar, Kankhal; Miskin Sambhaji, Ahmednagar; Mitra Sulakshana, Agartala; Mittal Ashok, Meerut; Mohammad Shamsuddin Molla, Sreerampur; Mohammed Muzaffar Sharif, Hyderabad; Mohan Rakesh, Ghaziabad; Mohanty Biswajit, Bhubaneswar; Mondal Nirpada, Raniganj; Mukherjee Basudeb, Chandan nagar; Mukundan Shyamala, Paryyanur; N Bhavani Prasad, Rajahmundry; N Kotresh, Bellary; N P Sharma, Ambikapur; NV Gopal Raju, Bhimavaram; NM Pickthall, Chennai; Nandi Ashok Kumar, Arambagh; Nigam Arun Kumar, Kanpur; PB Krishnamurthy, Nizamabad; P Hanumantha, Khammam; P Nagalingam, Huzurabad; P Arulkumar, Coimbatore; PK Gupta, Raigarh; Pal Supriya, Hindmotor; Palan Bharatkumar V, Mumbai; Pan Chandi Charan, Kolkatta; Pandit Prafulla, Nagpur; Panjwani Shaturghan, Indore; Pankaj Kumar, Raniganj; Pansari Ashok, Delhi; Panse Anil, Pune; Parashar Sanjay, Haridwar; Pardhi Chhagendra Kumar, M.P.; Pardhi

Chhagendra Kumar, M.P.; Parmar Nirml, Ahmedabad; Patel Anoop Chhaganlal, Mumbai; Patel Jitendra Bhogilal, Ahmedabad; Patidar Chensukh, Mandasaur; Patil Satish B, Belgaum; Paul Sanjoy, Coochbehar; Paul Shibendranath, Malda; Pawar Bharath, Nizamabad; Pm Nanjudappan, Coimbatore; R Mahendra, Shimoga; RP Chakravarty, Moradabad; R Rajesh, Bangalore; R Penchalaiah, Chennai; RL Agarwal, Raigarh; R S Naik, Durg; Rai Anurag, Deoria; Rai Ashok Kumar, Gorakhpur; Raut Dilip M, Thane; Rishikant Kumar, Ranchi; Roy Manjul Kumar, Kolkata; Roy Nikhil Ranjan, Kolkata; Roy Samit, Kolkata; S Bala Subrahmanyam, Vijayawada; S Dasgupta, Bakora; SK Chatterjee, Raipur; SK Dutta, Kolkata; SR Trivedi, Agartala; S Ranga Rao, Vijayawada; S Venkateswarlu, Khammam; SB Singh, Varanasi; SB Sunkad, Gulbarga; SK Biswas, Kolkata; SK Mandal, Bardhaman; S Prabhu Venkatesh, Dharapuram; ST Ahmad, Ranchi; S Varadharajan, Coimbatore; S Vidyasagar Reddy, Hyderabad; Sabnam Ali, Jiaganj; Sadhu Sumana Barua, Siliguri; Saha Chandan Kumar, Kolkata; Saha Hemsagar, Kalahandi; Saikia Amal, Biswanath; Saleem Kaiser, Raipur; Salve Ravindra R, Pune; Sana Sanjay, Kolkata; Sanghvi Rajnikant B, Mumbai; Sen Sujan, West bengal; Setabuddin Ahmed, Islampur; Shah Jaemin R, Vadodara; Shah Sandeep, Vadodara; Sharma Dayal, Bikaner; Sharma Pradeep Kumar, Assam; Shekhar Kumar, Ranchi; Sheth Dhaval, Vadodara; Shetiya Rasik M, Pune; Shetty Pravin, Mumbai; Shinde Chetan Anand V, Mumbai; Shyamal Kishore, Siwan; Singh Harajagindra, Assam; Singh Harikishor, Forbesganj; Singh Mithilesh, Bihar; Singh Rajiv, U.P.; Singh Ravindra Kumar, Bihar; Singh Rohit V, Thane; Sinha Arijit, Agartala; Sinha Pradeep Kumar, Ranchi; Solman Raju, Mancherla; Souren Misra, Malda; Srichandan Managobinda, Bhubaneswar; Srivastav SP, Lucknow; Sumalaykar, Kolkata; Sundesha Navratna, Mumbai; TVD Sasi Sekhar, Vijayawada; T Venugopal, Srikakulam; TC Debnath, Azimganj; T Suman, Warangal; Talukdar Jayanta, Howrah; Tewari Ajoy Bhaskar, Assam; Tewary Tirth Nath, Ranchi; Thavrani Chandrabhan, Akola; Tiwari Sonia, Allahabad; Tripathi Surya Kanta, Malda; Trivedishaival, Vadodara; Uvagare John, Ahmednagar; V Chandra Vasant, Mumbai; V K Agarwal, Balkeshwar; VSR Murthy, Hyderabad; V Seshagiri Rao, Srikakulam; VK Sinha, Ranchi; Vadukoot Francis, Kottakkal; Vaishnav Manmohan Sharan, Raipur; Valadra Usha, Surat; Varma Rajiv, Kolkata; Varshney Praveen Kumar, Aligarh; Vasudevan Sajeev, Chennai; Venkata Krishnaiah, Malur; Verma Mahendra, Delhi; Verma Manoj Kumar, Patna; Warnkar Premnath S, Coochbehar; Yadav Rajesh R, Mumbai.

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