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Transmission of SARS-CoV-2 infection in a large asymptomatic family cluster in Bihar state, India, 2020

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Abstract
We describe the spread of SARS-CoV-2 infection in an asymptomatic family case cluster by an asymptomatic index patient, occurred in March 2020 in India. All the confirmed cases neither had history of pre-existing or recent clinical presentations of acute respiratory illnesses, nor reported with development of symptoms during monitoring.

Keywords: SARS-CoV-2 infection, COVID-19, family cluster, Asymptomatic, super-spreader, transmission

Introduction
An ongoing global epidemic of novel coronavirus (SARS-CoV-2), was first reported from Wuhan, China (1). As of April 15, 2020, it has spread globally to over 210 countries (2) with 8,708,008 confirmed cases and 461,715 deaths (3). Since the first detection in January 30, 2020, SARS-CoV-2 cases in India has increased substantially with 410,461 confirmed cases and 13,254 deaths till June 21, 2020 (3).
In this first report from India, we describe the spread of SARS-CoV-2 infection in a unique asymptomatic family case cluster by an asymptomatic index patient that occurred in April 2020 in rural areas of Siwan district of Bihar, India. Our epidemiological investigation was reviewed and approved by the Ethics board.

Methods
Contact tracing is the course of identifying, assessing, and managing people who have been exposed to a disease to prevent transmission. As per ICMR guidelines, people who may have been exposed to the virus are to be followed for 28 days from the date of the probable last exposure/arrival from affected countries. We employed standard methods for contact tracing the index patient as per ICMR guidelines. The guidelines suggest that, "any person who has had contact with the index patient under investigation/treatment for suspected, probable or confirmed case of SARS-COV-2, should be monitored for the appearance of symptoms." The definition of a 'contact' is as follows: "Anyone who has provided care for the suspect or confirmed case, including a health care worker (including those involved in cleaning, waste management, laboratory technicians, doctors) or family member, or anyone who had close physical contact; anyone who stayed at the same place (lived with, or visited) while the index patient was symptomatic." Thus contact tracing of the index patient help in efficient surveillance of cases and contacts.
Notably, this index patient (Patient 1), a 33-year-old migrant worker from Oman, had no symptoms of acute respiratory illness, viz. fever, sore throat, coughing, wheezing or shortness of breath and seemed otherwise healthy. Eventually, he cleared the COVID-19 screening test at the airport and was home quarantined for two weeks, owing to his travel history. As per the patient's self-report, he had violated the quarantine directive and moved openly in the community in Siwan. On being informed by the locals, the Bihar COVID-19 team tracked, collected his sample and was confirmed as SARS-CoV-2 positive case on April 03, 2020. He was immediately transferred to the district isolation centre for active monitoring of symptom development. We started the process of tracing his contacts and confirm human-to-human transmission, if any (Figure 1).

Results and Discussion
As per our investigation, all the confirmed cases had no history of pre-existing and/or recent clinical presentations of acute respiratory illnesses or any travel history (except for Patient 1; Table 1) and the confirmed cases also did not develop any clinical symptom during the isolation period. We credited the infection to a potential super-spreader asymptomatic traveller who had flown back to India from Muscat on March 22, 2020. So far, he did not develop any clinical symptom for acute respiratory illness.
While contact tracing, we found that the house of this family is a huge double-storied concrete building with thirty-three family members. After initial interrogation, nasopharyngeal and/or oropharyngeal plus blood samples of the suspected contacts (members of the family, extended family and near neighbours), were collected in three phases and transferred to the diagnostic laboratory. Till April 01, Patient 1 had played cricket with his cousins, attended dinner parties, visit his neighbours and relatives who lived nearby to their house. As per the contact-tracing strategy, the samples were collected from the immediate family members of patient 1 (his wife, children, father, mother, brother, sister-in-law, nieces and nephews) in phase-1, where three were tested positive on April 6. On further tracing for more contacts in phase-2, ten positive cases were found on April 8 among his uncle, aunts, cousins and two neighbours. Next, the neighbours and relatives from the extended family were screened and interviewed in phase-3. Seven positive cases were confirmed on April 9 from these samples. Therefore, a

total of twenty-three samples were tested positive for SARS-CoV-2 signature markers by Real-time PCR (RT-PCR) diagnostic facility.

The routine laboratory investigation results were unremarkable and with no evidence of invasive lesions in the chest radiographs of the index patient or his contacts. The confirmed cases (seventeen females and six males) contained: fourteen members within the family plus nine cases among their neighbours and extended family members (Table 1). All the confirmed cases were extensively interviewed, but they did not report any prodromal or other symptoms before or after the arrival of Patient 1. All were immediately transferred to the isolation ward of the hospital for symptom monitoring. About 150 more villagers have been quarantined in a local medical facility. The village in Siwan district has now been sealed and surveillance on their movement has been intensified by the local government.

In self-report, the positive cases informed to have interacted with Patient 1 and Patient 2 and/or Patient 4. On further investigation, the source of infection in this cluster seemed to be primary (by patient 1) and/or secondary (by patient 2) and/or tertiary (by patient 4) exposure of the contacts (Figure 1). It is not clear why the small children of the family were not affected by the virus. The rest of the family members were negative in the testing and have been home-quarantined as per standard protocol. This village in Siwan district has now been sealed and surveillance on their movement has been intensified by the local government.

Contact tracing has gained much importance in the SARS-CoV-2 pandemic scenario, as it results in potential informations on person-to-person transmissibility of COVID-19. The transmission dynamics of this novel virus through pre-symptomatic and true asymptomatic patients is interesting. Some of the previous reports from China for human-to-human transmission of SARS-CoV-2 in family clusters either consisted of symptomatic index case with symptomatic and asymptomatic family members (2) or was by pre-symptomatic carriers (3, 4). Our report can contribute important information to SARS-CoV-2 epidemiology as true asymptomatic carriage may be a crucial contributor for transmission of SARS-CoV-2 infection in familial settings. This warrant designing of well-planned community-based surveillance strategies for contact tracing and control of super-spreading events.

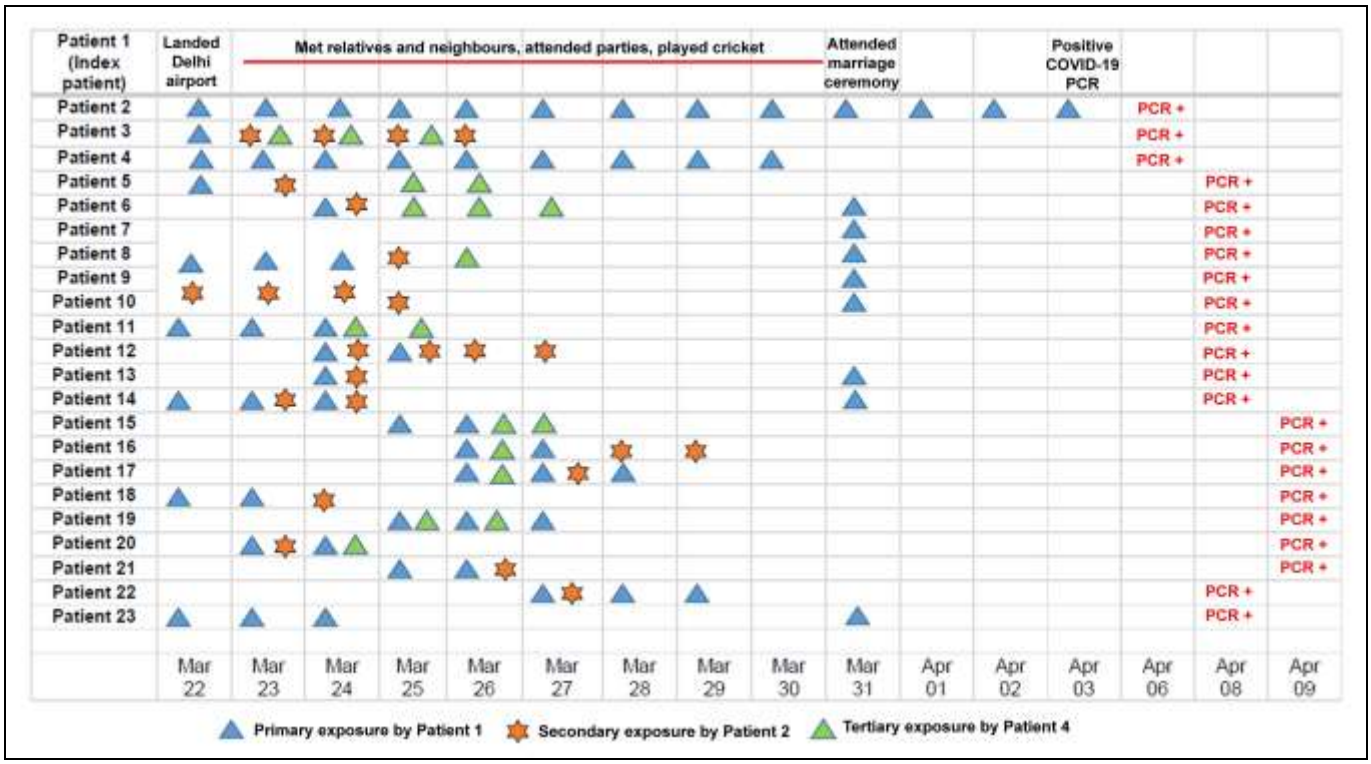

Fig 1

Table 1: Detailed characteristics of COVID 19 confirmed cases in the family cluster

Patient number	Age (years)	Gender	Relation with Patient 1	Travel and/or visit History #	COVID-19 result	Other respiratory viruses ##	Serological tests ###	Clinical Symptoms §	Clinical signs §§	Underlying medical conditions §§§	Treatment support requirement §§§§	Antivirals used	Placed in the isolation ward in the hospital	Symptom development during active monitoring *
Patient 1	33	M	NA	Yes	Positive	No	No	No	No	No	No	No	Yes	No
Patient 2	22	F	Wife	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 3	26	F	Sister-in-law	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 4	45	F	Mother	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 5	30	M	Uncle	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 6	29	F	Aunt	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 7	26	M	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 8	18	F	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 9	12	F	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 10	20	F	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 11	50	F	Aunt	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 12	20	F	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 13	12	F	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 14	10	M	Cousin	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 15	60	M	Neighbour	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 16	25	F	Neighbour	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 17	22	F	Neighbour	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 18	19	F	Relative	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 19	19	F	Relative	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 20	11	F	Relative	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 21	12	F	Relative	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 22	34	F	Neighbour	No	Positive	No	No	No	No	No	No	No	Yes	No
Patient 23	19	M	Neighbour	No	Positive	No	No	No	No	No	No	No	Yes	No

Travel and/or visit history denotes travel to areas during 14 days prior to testing like Wuhan (China) or to a location or community where transmission of SARS-CoV-2 disease is present or visit to any hospital where COVID-19 confirmed cases were admitted.
Other respiratory virus testing was for influenza, parainfluenza, rhinovirus, adenovirus and respiratory syncytial virus
Serological testing was for human immunodeficiency virus, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*.
§ Clinical symptoms denotes fever at evaluation, history of fever, pleuritic chest pain, sore throat, cough, breathlessness, nasal congestion, nasal discharge, myalgia, headache, abdominal pain, vomiting, diarrhoea, nausea, haemoptysis.
§§ Clinical signs denotes wheeze, nasal flaring, stridor, crepitation, lower chest indrawing, accesary muscle use.
§§§ Underlying medical condition denotes COPD, bronchitis, malignancy, chronic renal disease, diabetes, heart disease, hypertension, asthma (on verbal enquiry from patient)
§§§§ Treatment support denotes requirement of oxygen, ventilation, CPAP, bronchodilators, steroids, antibiotics.
*Till May 14, 2020

Author contributions
Concept and design: SD; Acquisition, analysis of data: AK, AS, SK, Interpretation and analysis of data: AS, SD; Interpretation of patients' hospital records: AKS, KP, RT; Drafting of manuscript: SD; Critical revision of manuscript: KP, RT, AS; Administrative, Technical and material support: PD; Supervision: PD

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