REVIEW

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# Secondary attack rate of COVID-19 in household contacts: a systematic review

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#### Summary

Coronavirus disease 2019 (COVID-19) is a novel virus with continuously evolving transmission trends. Contact tracing and quarantining of positive cases are chief strategies of disease control that has been accepted globally, though scientific knowledge regarding household transmission of the COVID-19 through contact of positive case is sparse. Current systematic review was planned to assess global statistics and characteristics of household secondary attack rate (SAR) of COVID-19. Eligible articles were retrieved through search of—MEDLINE, SCOPUS and EMBASE for the period December 2019 to 15 June 2020. Search terms were developed to identify articles reporting household SARs in various countries. After initial screening of 326 articles, 13 eligible studies were included in the final evidence synthesis. We found that SAR varies widely across countries with lowest reported rate as 4.6% and highest as 49.56%. The rates were unaffected by confounders such as population of the country, lockdown status and geographic location. Review suggested greater vulnerability of spouse and elderly population for secondary transmission than other household members. It was also observed that quarantining and isolation are most effective strategies for prevention of the secondary transmission of the disease. Symptomatic status of the index case emerged to be a critical factor, with very low transmission probability during asymptomatic phase. Present review findings recommend that adequate measures should be provided to protect the vulnerable population as only case tracing and quarantining might be insufficient. It should be combined with advisory for limiting household contacts and active surveillance for symptom onset.

#### Introduction

In December, 2019 Wuhan, China has reported first case of novel coronavirus infection and soon after that coronavirus disease 2019 (COVID-19) epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has progressed rapidly into a pandemic.<sup>1</sup> With this virus affecting millions of lives within short period of time, global scientific community has directed mammoth of efforts in understanding the disease, identifying the factors associated with transmission, discovering novel treatment molecules and developing diagnostics tools with greater  $\operatorname{accuracy}^{2,3}$ 

Though relatively limited, current understanding of disease showed active tracking of infected cases, quarantining/isolating the affected ones and their close contacts and screening of contacts for presence of disease as few of the most effective strategy for breaking the chain of virus transmission.<sup>4,5</sup> However, the effectiveness of these strategies enormously depends on the disease severity of an affected individual, time of contact, age and comorbid condition of the contact.<sup>6–8</sup> Till date it is known that elderly and patients with comorbid conditions are

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most vulnerable population for infection and poorer outcome.<sup>6,8</sup> However, the current global data showed that COVID-19 transmission dynamics are far more complex with multifactorial effect exerted by numerous influencers. Some preliminary contact-tracing studies have showed that the highest-risk exposure setting of COVID-19 transmission was the household contacts of the infected cases.<sup>9,10</sup> Even after national lockdowns and extreme social-distancing norms imposed by various nations, they still experience steep escalation in COVID-19 cases that may been substantially contributed by household transmission.

In epidemiology, a household secondary attack rate (SAR) is defined as number of household cases occurring within the incubation period upon exposure to a primary case divided by total susceptible household contacts. The current systematic review aims to study and document global statistics on SAR of COVID-19 among household contacts and identify its determinants, transmission triggers and epidemiological characteristics across various geographies. The household contacts included in the present review are defined as individuals sharing the same living address with the positive cases. This may contribute significantly in designing and developing infection control and prevention policies for COVID-19 that can limit further spread/ transmission of the disease.

#### Materials and methods

#### Search strategy

The current protocol-driven systematic review was undertaken to study and understand SAR of COVID-19 and identify key characteristic of this transmission in household contacts. For the review, we used the recommended method for systematic reviews and reporting based on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The 'Cochrane Handbook for Systematic Reviews of Interventions' was followed for planning and conducting the review.<sup>11,12</sup>

#### Search strategies and selection criteria

The articles were retrieved from three databases-MEDLINE (through PubMed and CENTRAL), EMBASE and Scopus using the keywords representing COVID-19 and SAR. The key search terms used were 'COVID-19' OR 'Coronavirus' OR 'SARS-CoV-2' AND 'Household contacts' AND 'Secondary attack rate' OR 'Secondary transmission'. Google scholar search was also under taken to identify relevant gray literature using the same search terms. Additionally, we also screened WHO and UNICEF databases for identification of potentially relevant studies reporting household SAR of COVID-19. The reference lists of all the included articles were explored to retrieve related articles. Two reviewers (K.S. and D.S.) independently assessed the databases for screening of the articles, which were published during December 2019 to 15 June 2020 using title and abstract. The review included only articles published in English language, in indexed peer-reviewed journals. Articles available in Chinese language were included only if summary was published in English language. The final exclusion of the studies and data extraction were undertaken by both the authors after assessing full texts of the articles. Any discordance between the authors was settled by discussion and any difference of opinion arose was resolved through mutual consensus

After initial screening, identified articles were checked for duplication, and the remaining articles were evaluated for exclusion and inclusion based on pre-defined criteria. Studies not reporting quantitative statistics regarding SARs, providing SARs in close contacts but not in household contacts, were excluded from evidence synthesis. The remaining articles were assessed for potential inclusion where studies with unclear reporting were excluded. Details of the studies, databases searches were exported to an excel file and 30% of the excluded studies were cross verified by one reviewer. The entire screening process and study selection is presented as PRISMA diagram in Figure 1.

#### Data extraction and data synthesis

A computerized data extraction tool was developed to prepare the data collection matrix. For generalizability, this electric data collection matrix was used by all the reviewers. One reviewer (K.S.) extracted data from included studies into predesigned data extraction form and other reviewers (D.S. and D.M.) crosschecked the data. Each included study was assessed for retrieval of the following: authors, title, study year, country, study design, details of participants screened, type and number of primary cases, SAR proportion, determinants of SAR, study duration, type and total number of household contact and any other key findings of the study. The information regarding above mentioned parameters was extracted from each article in a descriptive manner and it was reported using the descriptive statistics (frequency and percentage) from the coded data matrix or as narrative findings. Studies were explored for reporting of granular data regarding determinants of SAR and were combined if the data were found appropriate and adequate.

#### Results

The systematic review included 13 articles reporting SAR in various countries and population.<sup>13–24</sup> This was achieved through series of screening processes as mentioned in PRISMA diagram. Out of 13, one article undertook modeling study to predict SAR and one review summarized SAR from nine independent reports.

#### Characteristic details of the included studies

Descriptive details of the studies were assessed and are summarized as Table 1. As the pandemic first affected China and infected others eventually, majority of the studies (57%) were reported from various parts of China followed by Korea. The primary cases pool used in the included studies were principally symptomatic confirm cases of COVID-19, some studies also included asymptomatic confirm cases as well (n = 4), though they were limited in number. One large study reported from India using national data of 1021518 included both symptomatic and asymptomatic high-risk-contacts, however they clearly reported the role of changing guidelines into screening of asymptomatic cases. The studies reporting SARs in bothhousehold contact along with non-household contact was also included to identify key characteristic features of both, however detailed evidence synthesis included data of only household contacts. Total number of family contact in the reviewed studies ranged from 137 to 200006 with varying rate of secondary transmission in contacts.

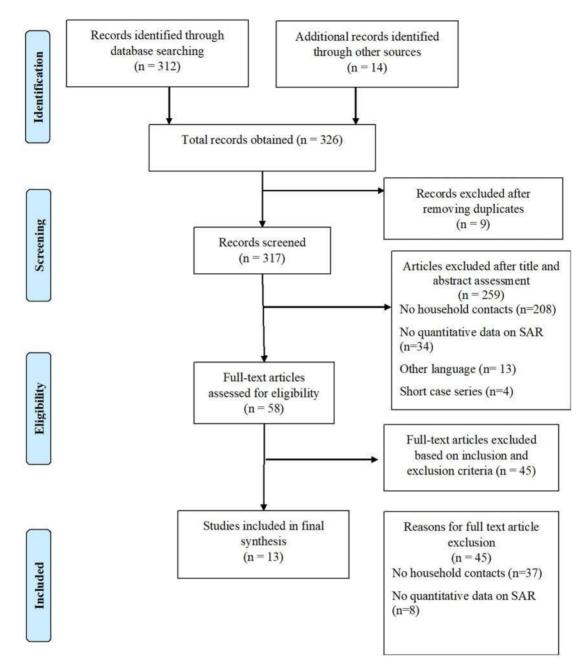


Figure 1. Flow diagram of study selection.

#### Secondary attack rate in household contacts of COVID-19

Details of SAR in household contacts were assessed from each study and found to be ranging between 4.6 and 49.56% (Table 2). The rate did not show any correlation with geographic region, time of lockdown imposition or overall population of the country. Majority of the studies reported SAR data till late March 2020, only one study from Indian Council of Medical Research (ICMR), India, showed national data recorded till 30 April 2020. Values of 95% confidence interval of the SAR were also noted and mentioned for each study; however, few studies did not provide it.

## Key characteristic features of household transmission of COVID-19

Articles were further studied in detail to identify the transmission characteristics of the virus in household contacts and the following key observations were found and are mentioned in Table 3. Diagrammatic representation of SAR in household contact is presented as Figure 2.

- Household contacts of the laboratory confirmed cases have higher SAR in contrast to other 'close contacts'.<sup>16</sup> The confirmation of the cases was based on the diagnostic protocol of the respective country. However, nucleic acid test (reverse transcription polymerase chain reaction) is globally accepted method of diagnostic, may/may not be coupled with radiography findings. Primary cases were dominated by adult population with more proportion of elderly having comorbid conditions.
- Spouses and elderly are more prone to SAR than younger population (supported through reported odds). Minors (<18/<20 years) are at lower risk of SAR.<sup>16,22</sup>

Sr. no.	Author	Title	Country	Type of primary cases details	Number of primary case	Type of contacts	Number of contacts	SAR (%) in contacts
-1	Abraham et al. <sup>13</sup>	Laboratory surveillance for SARS-CoV-2 in India: per- formance of testing and descriptive epidemiology of detected COVID-19, 22 January to 30 April 2020	India	Symptomatic sus- pected cases and certain asymp- tomatic groups (high risk)	40 184	All contacts	<ul> <li>(1) 200 006 (19.6%) asymptomatic family con- tacts(2) 48 852</li> <li>(4.8%) asymp- tomatic health- cora workers</li> </ul>	6% (95% CI, 5.4–8.1%)
5	Bi et al. <sup>14</sup>	Epidemiology and trans- mission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retro- spective cohort study	China	All confirmed cases	391	Close house- hold contacts	1286 (686 house- hold contacts/ 456 others)	11.20% (95% CI, 9.1– 13.8%)
m	Burke et al. <sup>15</sup>	Active monitoring of per- sons exposed to patients with confirmed COVID- 19—USA, January- February 2020	ASU	Travelers	10	Any contact including household contact	445 contacts 19 (4%) house- hold contact	<ul> <li>(1) All contacts: 0.45%</li> <li>(95% CI, 0.12-1.6%)</li> <li>(2) Household contacts: 10.5% (95% CI, 2.9-31.4%)</li> </ul>
4	Cheng et al. <sup>16</sup>	Contact-tracing assessment of COVID-19 transmis- sion dynamics in Taiwan and nisk at different ex- posure periods before and after symptom onset	Taiwan	Confirmed cases	100	Contact with household, family, and health care	2761	Overall, 0.7% (95% CI, 0.4–1.0%); household contact, 4.6% (95% CI, 2.3–9.3%); non-house- hold family contact, 5.3% (95% CI, 2.1– 12.8%); healthcare contact, 0.9% (95% CI, 0.4–1.9%); others, 0.1% (95% CI, 0–0.3%)
Ŋ	Korea Centers for Disease Control and Prevention, Cheongiu, Korea <sup>17</sup>	Coronavirus disease-19: summary of 2370 contact investigations of the first 30 cases in the Republic of Korea	Republic of Korea	Symptomatic con- firmed, asymptomatic	30	Household contacts	2370	Household contact, 7.56% (95% Cl, 3.7– 14.26%); overall, 0.55% (95% Cl, 0.31–0.96%)
Q	Jing et al. <sup>18</sup>	Contagiousness and sec- ondary attack rate of 2019 novel coronavirus based on cluster epidem- ics of COVID-19 in	China	Symptomatic con- firmed, asymptomatic	349	Household contacts		49.56% (95% CI, 43.02– 56.10%)

Table 1. C	<b>Table 1</b> . Continued							
Sr. no.	Author	Title	Country	Type of primary cases details	Number of primary case	Type of contacts	Number of contacts	SAR (%) in contacts
2	Jing et al. <sup>19</sup>	Household secondary at- tack rate of COVID-19 and associated determinants	China	Primary and sec- ondary cases	212	Household contacts		Household contacts, 13.8% (95% CI, 11.1– 17.0%); non-household contacts, 3.1% (95% CI, 4.7–10.6%)
Ø	Jing et al. <sup>19</sup>	Household secondary at- tack rate of COVID-19 and associated determinants	China	Primary and sec- ondary cases	349	Household contacts	1938	19.3% (95% CI, 15.5– 23.9%)
თ	Kwok et al. <sup>20</sup>	Epidemiological character- istics of the first 53 la- boratory confirmed cases of COVID-19 epidemic in Hong Kong, 13 February 2020	China	Confirmed cases	53	Household and visitors		11.7% (95% CI, 7.61– 16.8%)
10	Liu <sup>21</sup>	Secondary attack rate and superspreading events for SARS-CoV-2	UK	Primary cases		Household and close contacts	137	35% (95% CI, 27–44%)
11	Li et al. <sup>22</sup>	The characteristics of household transmission of COVID-19	China	Primary cases	105	Household	392	16.30%
12	Park et al. <sup>23</sup>	Coronavirus disease out- break in call center, South Korea	South Korea	Primary cases	97	All contacts	225	Household contacts, 16.2% (95% CI, 11.6– 22.0%)
13	Sun et al. <sup>24</sup>	Epidemiological character- istics of 2019 novel cor- onavirus family clustering in Zhejiang Province	China	Symptomatic index and asymptomatic confirmed cases	181	Household		31.68%

I able 2. Hou	senold SAK as per coul	Table Z. Household SAK as per country, population, lockdown, and caseload.	wn, and caseload					
Sr. no.	Author	Country	Country population <sup>a</sup>	Time of lockdown start	Study included patients till	Total cases recorded till study period	Region	Household SAR (%)
1	Abraham et al. <sup>13</sup>	India	135.26 crores	25 March 2020	22 January to 30 April 2020	71 493	South Asia	6% (95% CI, 5.4– 8.1%)
5	Bi et al. <sup>14</sup>	China	139.27 crores	23 January 2020	14 January to 12 February 2020	2068	East Asia and Pacific	11.2% (95% CI, 9.1–13.8%)
3	Burke et al. <sup>15</sup>	USA	32.82 crores	23 March 2020	26 February	870	North America	10.5% (95% CI, 2.9–31.4%)
4	Cheng et al. <sup>16</sup>	Taiwan, China	139.27 crores	23 January 2020	15 January to 18 March	12 018	East Asia and Pacific	4.6% (95% CI, 2.3–9.3%)
'n	Korea Centers for Disease Control and Prevention, Korea. <sup>7</sup>	Republic of Korea	5.16 crores	No lockdown	24 January and 10 March	4125	East Asia and Pacific	7.56% (95% CI, 3.7-14.26%)
9	Jing et al. <sup>18</sup>	China	139.27 crores	23 January 2020	18 February 2020	1903	East Asia and Pacific	49.56% (95% CI, 43 07–56 10%)
7	Jing et al. <sup>19</sup>	China	139.27 crores	23 January 2020	15 April 2020	70 053	East Asia and Pacific	13.8% (95% CI, 11.1–17.0%)
8	Jing et al. <sup>19</sup>	China	139.27 crores	23 January 2020	02 April 2020	72 846	East Asia and Pacific	19.3% (95% CI, 15.5–23.9%)
6	Kwok et al. <sup>20</sup>	China	139.27 crores	23 January 2020	13 February 2020	1826	East Asia and Pacific	11.7% (95% CI, 7.61–16.8%)
10	Liu <sup>21</sup>	UK	6.66 crores	23 March 2020	February 2020	544	Europe and Central Asia	35% (95% CI, 27– 44%)
11	Li et al. <sup>22</sup>	China	139.27 crores	23 January 2020	15 March 2020	267	East Asia and Pacific	16.30%
12	Park et al. <sup>23</sup>	South Korea	5.16 crores	No lockdown	March 2020	57 655	East Asia and Pacific	16.2% (95% CI, 11.6–22.0%)
13	Sun et al. <sup>24</sup>	China	139.27 crores	23 January 2020	10 February 2020	267	East Asia and Pacific	31.68%

Table 2. Household SAR as per country, population, lockdown, and caseload

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<sup>a</sup>As per the year 2018.

.011.10	Author	Key findings reported in studies
4	Abraham et al. <sup>13</sup>	<ol> <li>After sensitivity analysis addressing mission data SAR changed from 6 to 3.9%</li> <li>After correction, secondary attack rate was highest in Chandigarh (11.5%) and Maharashtra (10.6%)</li> <li>95% of secondary cases were expected to develop symptoms within 14.3 days (95% CI. 11.1–17.6%) of their infector</li> </ol>
7	Bi et al. <sup>14</sup>	<ul> <li>(1) Household contacts and those traveling with a case were at higher risk of infection (odds ratio 6.27 [95% CI, 1.49–26.33%] for household contacts and 7.06</li> <li>[1.43–34.91%] for those traveling with a case) than other close contacts</li> <li>(2) At the time of the first clinical assessment, 25 (29%) of 87 cases in the contact-based surveillance group did not have fever, and 17 (20%) of 87 had no</li> </ul>
64	Burke et al. <sup>15</sup> Cheng et al. <sup>16</sup>	symptoms Five household contact who continued exposure to COVID-19 during quarantine phase did not developed infection (1) The attack rate was higher among contacts whose exposure to the index case started within 5 days of symptom onset than those who were exposed later (2) The attack rate was higher among household (4.6% [95% CI, 2.3–9.3%)) and non-household (5.3% [95% CI, 2.1–12.8%)) family contacts than that in health care
		or other settings (3) The attack rates were higher among those aged 40–59 years (1.1% [95% CI, 0.6–2.1%]) and those aged 60 years and older (0.9% [95% CI, 0.3–2.6%]) (4) Odds of SAR is higher in contacts of cases with severe symptoms as compared to cases with mild symptoms
	Korea Centers for Disease Control and Prevention, Cheongju, Korea. <sup>17</sup>	(1) Odds of SAR is higher in household contacts as compared other contacts (healthcare workers and co-workers) (2) Identified household transmission as one of the major drivers of SAR
9	Jing et al. <sup>18</sup>	<ul> <li>(1) The secondary attack rate in close contacts with shortest incubation period of 1–3 days was 17.12–18.99%, the secondary attack rate in family members was 46.11–49.56%(2) The median number of subsequent infections caused by an index case in a cluster epidemic was 3</li> <li>(3) Infection ratio of family member transmission was 85.32% (1.86/2.18)</li> </ul>
	Jing et al. <sup>19</sup>	<ul> <li>(1) The attack rate for household contacts from index cases was 12.6% while it was 3.1% for non-household contacts</li> <li>(2) The household attack rate was lower among contacts &lt;20 years (5.3%, 95% CI, 2.4-9.8%) compared to older age groups (13.7% among 20-59-year olds [95% CI, 10.7-17.2%] and 17.7% among those 60 years or older [95% CI, 1.9-24.8%])</li> <li>(3) Mean incubation period of 4 days and maximum infection period of 13 days</li> </ul>
	Jing et al. <sup>19</sup>	<ul> <li>(1) Within households, the non-primary attack rate was much lower in contacts &lt;20 years group, 5.26% (95% CI, 2.43–9.76%), as compared to 13.72% (95% CI, 10.Within household 5.95% (95% CI, 11.89–24.83%) in 20–59-year olds and ≥60-year olds, respectively (P-values &lt;0.005). No difference in gender</li> <li>(2) Estimated the household SAR to be 13.8% (95% CI, 11.1–17.0%) if household contacts are defined as all close relatives and 19.3% (95% CI, 15.5–23.9%) if household contacts are defined as all close relatives and 19.3% (95% CI, 15.5–23.9%) if household contacts of the household SAR to be 13.8% (95% CI, 11.1–17.0%) if household contacts are defined as all close relatives and 19.3% (95% CI, 15.5–23.9%) if household contacts of the same residential address as the cases. On average, a COVID-19 case infected 0.48 (95% CI, 0.39–0.58) close contacts</li> </ul>
9 10	Kwok et al. <sup>20</sup> Liu <sup>21</sup>	The comparatively low secondary attack rate in Hong Kong might be attributable to the high level of civil engagement in individual-level preventive measures (1) More data are needed to reliably estimate the true within-household and between-household transmission for COVID-19 (2) An infection with a high household SAR but a modest R0 would suggest that the transmission is driven by a relatively small number of high-risk contacts. A large household SAR further suggest that between-household transmission risk is lower; otherwise the observed R0 would be larger
11	Li et al. <sup>22</sup>	<ol> <li>SAR in children, 4%, adults, 17.1%</li> <li>Quarantining of index cases reduced SAR from 16.9 to 0%</li> <li>Spouses of index cases are at higher risk of developing SAR</li> </ol>
12 13	Park et al. <sup>23</sup> Sun et al. <sup>24</sup>	Hore the fourth of a symptomatic cases did not develop SAR (1) Family secondary attack rate for subsequent cases and asymptomatic infected cases is 31.61 and 43.20%, respectively (2) The family secondary attack rate of the spouses of the family index cases is 63.87%, is higher than that of their children (30.53%), parents (28.37%), and other family members (20.93%), the difference was statistically significant

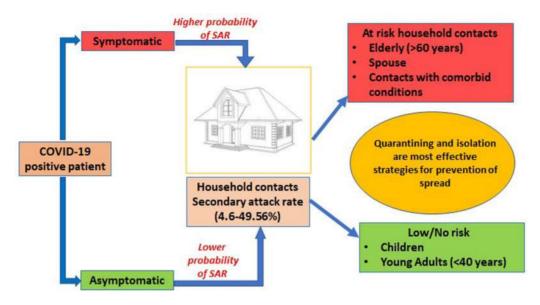


Figure 2. Diagrammatical presentation of household transmission of COVID-19.

- Positivity rate is highest among symptomatic contacts. High transmissibility of COVID-19 before and immediately after symptom onset.<sup>22,23</sup>
- Correction for missing case and confounder effect changes the rate of secondary attack.<sup>13</sup>
- Increased frequency of contact is directly related to SAR rate.<sup>22</sup>
- Significant proportion (50–95%) of contacts did not develop infection in spite of continued contact with positive case that indicates possible role of natural immunity or resistance to disease.<sup>13–24</sup>
- Mean incubation period among household contacts that developed the disease varies widely across the studies.
- The median number of subsequent infections caused by an index case in a cluster epidemic is around 3 and mean of around 2 cases.<sup>19</sup>
- Isolation/quarantining of index cases (immediately after symptom onset) have resulted in reduced risk of SAR.<sup>22,23</sup>
- The median time from symptom onset in index cases to symptom onset in household contacts varies widely, though it is 6 days approximately.<sup>22</sup>
- Only one study mentioned median household size as four people (inter quartile range: 3–6).<sup>22</sup>
- Index cases with fever resulted in more SAR as compared to asymptomatic or index cases with mild symptoms.<sup>19</sup>
- Few studies stated lack of transmission before symptom onset (in asymptomatic state).<sup>22,23</sup>

#### Discussion

This systematic review assessed reported statistics of SAR across the globe and studied various aspects of secondary transmission in household contacts. It was found that household contacts are at greater risk of SAR as compared to other contacts such as healthcare workers and workplace contacts.<sup>14</sup> We observed that the household SARs varies widely with one study in Taiwan 4.6% (95% CI, 2.3–9.3%) showing lowest incidence and again China reporting the highest incidence 49.56%.<sup>16,18</sup> However, majority of the articles reported SARs below 20% (71% studies), only three articles showed the higher rates (above

30%). Out of these three, two studies were from China and were showing SAR of 49.56 and 31% and third was from UK (35%).<sup>18,24</sup> Potential explanation for this higher rate could be the fact that the data were compiled till 10 and 18 February, respectively, and that time the country was experiencing peak of the transmission with  $\sim$ 15000 newly diagnosed cases in a day. Studies acknowledged the higher rate of family renewal rate of cluster contacts (higher than all contacts) and clearly stated that in the early stage of epidemic prevention and control in many areas of the country, non-single/single room isolation measures were taken for close contacts, which cannot effectively cut off the transmission route within the family. In case of third study reporting 35% of SAR was calculated by cumulative analysis of nine datasets that involved meal, home, restaurants and other contacts and hence may show have introduced some bias in the household contact statistics.<sup>22</sup> Authors also mentioned that an infection with a high household SAR but a modest R0 would suggest that the transmission is driven by a relatively small number of high-risk contacts. A large household SAR further suggests that between-household transmission risk is lower; otherwise the observed R0 would be larger.

Another significant observation from this systematic review is the identification of the vulnerable individual in household for COVID-19. Spouses and elderly population evidently emerged as one of the most susceptible groups for secondary transmission, and the difference in SAR of these groups with other family members was statistically significant.<sup>16,22</sup> Odds of SAR was almost three times higher (~13-15) in population ageing >60 years as compared to their younger counterparts (<20 years), where odd was nearly 5. SAR in spouses of indexed cases ranged from 27.8 to 63.87% and stated as considerably higher than children and other adult members of the family. This could be possibly due to their active involvement in the care taking activities of the cases that may have resulted into prolonged very close physical contact with the index cases and hence longer exposure to the virus.<sup>25,26</sup> It is known that old age and comorbid conditions are independent risk factors of COVID-19 infections and hence it explains higher transmission rate in elderly in household SAR as well.  $^{27-3\bar{0}}$  This resulted in higher fatality rate in elderly as well.  $^{\rm 8,31-35}$  It was found that SARs in asymptomatic contacts were significantly lower than the household contacts of the symptomatic cases, where time for symptom onset in index case did not alter the rate of secondary transmission in contacts.<sup>23</sup> Li et al.<sup>22</sup> showed that the median time from symptom onset in index cases to symptom onset in household contacts was 6 days, though it varied somewhat from study to study. Hamner et al. suggested that persons infected with COVID-19 are most infectious from 2 days before through 7 days after symptom onset.<sup>36</sup> Cheng et al. also suggested that transmission probabilities are highest during first five days of the symptoms onset as compared to later exposures.<sup>16</sup> Recently WHO also released a statement indicating that asymptomatic carriers spreading COVID-19 is a rare phenomenon, however later they clarified the statement mentioning need for more data to substantiate it further (http://www.emro.who.int/health-topics/corona-virus/transmission-of-covid-19-by-asymptomatic-cases.html).

Right from the initial outbreak of the COVID-19, epidemiologists and public health experts undoubtedly recommended quarantining and isolation of the positive cases as one of the most effective preventive strategy.<sup>37,38,39</sup> Findings of this review showed that SARs in case of quarantining of index cases immediately after onset of symptoms were significantly low in case of non-quarantined index cases.<sup>22</sup> It reduced SAR to as low as to 0%. However, in spite of varying number of household contacts developing COVID infection, it is also true that significant number of individuals did not develop infection in spite of sharing the same household. They continued getting exposed to the index cases and no secondary transmission occurring in them that potentially indicates a role of individual-specific natural immunity for resistance to COVID-19 that need to be evaluated further.<sup>15</sup>

Though to the best of our knowledge this is first systematic review documenting household SARs of COVID-19 in various geographic regions and assessing its clinical characteristics, it suffers from some inherent limitations. As the pandemic caught majority of the country's health system unaware and unprepared, there are major data gaps and that may have contributed in missing data bias in calculation of SARs.40 Some of the included studies have mentioned this as well and they tried to minimize the error by undertaking the sensitivity analysis that resulted in the considerable change in SAR.<sup>13</sup> However, majority of the studies did not perform this and reported the SAR based on the available data only. Similarly, with continuously evolving diagnostic guidelines there are several other confounders such as (i) country-specific differences in the diagnostic algorithms; i.e. in some part of the world, nucleic acid test along with radiography is used for COVID-19 diagnosis, whereas in some countries only reverse transcription polymerase chain reaction is being used that itself has limited sensitivity. (ii) Diagnostic and screening protocol that may/may not have recommend testing of asymptomatic cases and that may have resulted in under reporting of the SAR.<sup>41,42</sup> Though we also tried to assess potential role of lockdown on household transmission, we could not find any significant association between the both. Moreover, there are also possibilities that family members of the index cases may have come in contact with other positive cases outside their home as well and in those cases traveling and contact history are vital; however, very few studies discussed these confounders effects while deriving SARs.<sup>13</sup>

This study will help in developing policies and programs such as 'home isolation' to reduce spread of COVID-19 in the household contacts and through that spread in the community. However further detailed, prospective studies critically addressing intrafamily transmission of the disease are urgently needed.

#### Conclusion

Assessment of infectiousness of the COVID-19 cases during their early symptomatic phase is critical in designing preventive strategies for pandemic control. Household contacts of COVID-19 cases are most vulnerable population and need special attention especially when all the countries have imposed lockdowns and are advocating 'stay home'. The evidence synthesis yielded three key observations that may have potential implication for preventive policies: (i) most susceptible groups are spouses and elderly for secondary infection in home. Hence, it is crucial to advocate self-monitoring of the symptoms in this group. (ii) Asymptomatic cases have lesser chances of spreading the disease (low SAR); however, immediate quarantining of the cases upon development of the symptoms reduces the risk of SAR drastically. (iii) Contact time with the index cases has direct correlation with SARs and hence enough measures should be taken to limit this contact.

Conflict of interest: The authors declare that they do not have any affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript..

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