

1 **Age specificity of cases and attack rate of novel**
2 **coronavirus disease (COVID-19)**

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24 Age distribution of the cases with novel coronavirus disease (COVID-19) is rather
25 different from that of influenza. In China, there were few reported cases among children
26 [1] and serious or fatal child cases were also very infrequent. The age specificity is
27 particularly important in designing details of social distancing, including school closure,
28 as interventions, which is now recognized as the mainstream of interventions against
29 COVID-19. Investigating the details of contacts, substantial susceptibility among
30 children was demonstrated [2], but further insights into underlying mechanisms should
31 be explored. Here we examined the age distribution of COVID-19 cases in Japan from
32 January to March, 2020.

33

34 In Japan, a total of 313 domestically acquired cases have been confirmed as of 7 March
35 2020 (Figure 1). All these tested positive to reverse transcriptase polymerase chain
36 reaction (RT-PCR), and they arose from suspected cases with close contact (n=2496).
37 Male dominate confirmed cases (55.2%), and this finding is consistent with China [1].
38 Age category and gender were available for 173 male cases and 121 female cases. Out
39 of 173 male cases, seven were aged 0-19 years, 84 were aged 20-59 years and 82 were
40 aged 60 years and older, while three were aged 0-19 years, 69 were aged 20-59 years
41 and 49 were aged 60 years and older for female. It is remarkable that there are very few
42 child cases aged from 0-19 years in Japan.

43

44 Because all sample data stems from exposed and suspected individuals, age-specific
45 attack rate (AR) is calculable. Figures 1E and 1F show the AR estimates by age group
46 and gender. AR was very low, 7.2% (95% Confidence Interval (CI): 3.0%, 14.3%) and
47 3.8% (95% CI: 0.8%, 10.6%), respectively, among male and female children aged from

48 0-19 years. The peak AR was seen in those aged from 50-59 years both for male, 22.2%
49 (95% CI: 16.3%, 29.0%), and female, 21.9% (95% CI: 14.4%, 31.0%).

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51 What our short analysis shows is that children are less likely to be diagnosed as cases,
52 and moreover, the risk of disease given exposure among children appears to be low.

53 Both the overall risk and the conditional risk of disease given exposure are likely to be
54 the highest among adults aged from 50-69 years. The finding contradicts other widely
55 circulating respiratory viral infections, e.g. seasonal influenza and respiratory syncytial
56 virus infection, to which children are known to act as the focal host of transmission.

57 How can the age-specificity happen? The most plausible explanation that we believe is
58 immune imprinting to a similar virus among adults. Such virus must have continued to
59 circulate in the human population by 20 years ago, and may be most intensely circulated
60 by around 50 years ago. Severe acute respiratory syndrome-2 (SARS-2) coronavirus
61 may be antigenically closely related to the old coronavirus, and infected adults in the
62 present day may experience erroneous recognition of SARS-2 coronavirus. Although
63 not focusing on the age specificity, a hypothetical discussion took place, suspecting of
64 antibody dependent enhancement (ADE) as a potential biological mechanism of
65 heterogeneous risks of death [3], which could explain the diagnosis of severe cases in
66 higher age groups than in children, as seen in the present study.

67

68 In order to validate the hypothesis, it is ideal to conduct a seroepidemiological study
69 which may involve multiple candidate antigens including other coronaviruses [4].

70 Examining the age-dependent strengths of immune cross reactivity, immune imprinting

71 can be verified as the explanatory mechanism, which would have critical insights into
72 minimization of unavoidable deaths.

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80 **Authors' contributions**

81 All authors conceived the study and participated in the study design. K.M. collected and
82 analyzed the data. H.N. and K.M. drafted the manuscript and R.O. and K.M. revised the
83 the earlier versions of the manuscript. All authors edited the manuscript and approved
84 the final version.

85 **Conflict of interest**

86 The authors declare no conflicts of interest.

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104 **Figures**

105 **Figure 1. Age distributions of novel coronavirus disease (COVID-19)**

106 Age distributions of suspected individuals with close contact among male (A) and

107 female (B), respectively. Age distributions of laboratory-confirmed cases among male

108 (C) and female (D), respectively. Attack rate, i.e. cases out of suspected close contact, is

109 shown by gender (male (E) and female (F)).

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