Single Transverse Palmar Crease as a Potential Risk Factor for COVID-19

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Abstract: Aims: While South Asians in the United Kingdom suffer from higher mortality from COVID-19, the exact reason for the ethnic disparity is unknown. One solution is to find a genetic correlate of South Asian ethnicity and see if the same correlate is associated with an increased likelihood of COVID-19 contraction among Whites.

Methods: The author analyzed a prospectively longitudinal, nationally representative sample from the British Cohort Study that began at birth in 1970 and has information on COVID-19 health status in May 2020.

Results: Palmer crease patterns measured at age 10 were significantly associated with the likelihood of COVID-19 contraction and the number of symptoms at age 50. Individuals with single transverse palmar crease (STPC) on the right hand had 22.9% chance of contracting COVID-19 compared with 9.5% for those with the normal crease.

Conclusions: Because having STPC on the right hand nearly triples the odds of contracting COVID-19 among Whites, and South Asians are 4 to 5 times as likely to have STPC as Whites do, the genes for/chromosomal abnormalities associated with STPC might be one of the contributors to the higher mortality from COVID-19 among South Asians in the United Kingdom.

Key Words: Centre for Longitudinal Studies, coronavirus, palmar flexion creases, Sydney crease

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Since the beginning of the coronavirus pandemic in the United Kingdom, researchers have noted that members of certain ethnic groups, most notably Blacks and South Asians, had elevated risks of contraction of and mortality from COVID-19.[1,2] While the statistics on the ethnic disparities in the susceptibility to COVID-19 seems clear and beyond dispute, there is no agreement as to *why* such disparities exist. One significant problem is that race and ethnicity in the United Kingdom are statistically correlated and confounded with a host of social and economic factors such as social class, earnings, education, occupations, diet, access to health care, neighborhood of residence, and lifestyles. It is therefore difficult to tease apart the effects of biological and genetic differences between ethnic groups from associated social and economic factors as the true cause of elevated susceptibility to and mortality from COVID-19 among Blacks and South Asians.

One possible solution to this problem is to isolate a genetic or biological correlate of ethnicity and examine whether the same correlate increases susceptibility to COVID-19 in another ethnic group. For example, if South Asians have a higher probability of carrying a genetic variant or chromosomal abnormality X, and the same X is associated with an elevated risk for COVID-19 contraction or mortality among Whites, then we could be reasonably certain that X, rather than any of the social and economic factors, is at least a partial contributor to the higher risk of COVID-19 among South Asians.

One candidate for such a genetic instrument is the single transverse palmer crease (STPC). Single transverse palmer crease is one of the three major variants—STPC, Sydney, and Suwon—of the normal palmar crease currently recognized in human anatomy.[3] The STPC is four to five times as common among South Asians as among Whites; somewhere between 13% and 14.4% of South Asians have STPC, whereas only 3% of Whites do,[4] although it is not more common among Blacks than among Whites.[5] The STPC is also known to be associated with a large number of genetic and chromosomal disorders.[6] Thus, if STPC is significantly associated with susceptibility to COVID-19 among Whites, then it is strong evidence that it is the underlying genetic and chromosomal disorders that produce STPC, not any of the social and economic factors statistically associated with ethnicity, which partially explain the higher incidence of and mortality from COVID-19 among South Asians in the United Kingdom. Palmar flexion creases are entirely genetic in origin and form between the seventh and ninth week of gestation.[7] The STPC is also hereditary,[6] and thus, if it turns out that its genetic and chromosomal correlates are a risk factor in COVID-19, it can also explain why multiple deaths seem to occur frequently in clusters within different families. If this is the case, then physicians can use STPC as a diagnostic marker for higher susceptibility for COVID-19 *even in the absence of the knowledge of the precise mechanism by which the underlying genetic and chromosomal variants increase such susceptibility.* Very few studies have examined the association between different palmar creases and any medical or health outcome.

In this article, the author takes advantage of a unique dataset that has prospectively longitudinal data on a large, nationally representative sample of a population in the United Kingdom since birth to examine whether the higher incidence of STPC (and its underlying genetic and chromosomal abnormalities) can potentially explain the higher incidence of COVID-19 among South Asians in the United Kingdom. In particular, the author examines the statistical association between STPC and COVID-19 contraction within an entirely White sample.

METHODS

Data

The British Cohort Study (BCS), originally developed as the British Birth Survey and a sequel to the 1958 National Child Development Study, included all babies (n = 17,196) born in Great Britain (England, Wales, and Scotland) during the week of April 5–11, 1970. All surviving members of the cohort who still resided in the United Kingdom (Great Britain plus Northern Ireland) were subsequently reinterviewed in 1975 (Sweep 1 at age 5; n = 13,135), in 1980 (Sweep 2 at age 10; n = 14,875), in 1986 (Sweep 3 at age 16; n = 11,615), in 1996 (Sweep 4 at age 26; n = 9003), in 2000 (Sweep 5 at age 30; n = 11,261), in 2004 (Sweep 6 at age 34; n = 9665), in 2008 (Sweep 7 at age 38;

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The data and materials used in the research are freely available to registered users of the UK Data Service at https://ukdataservice.ac.uk/.
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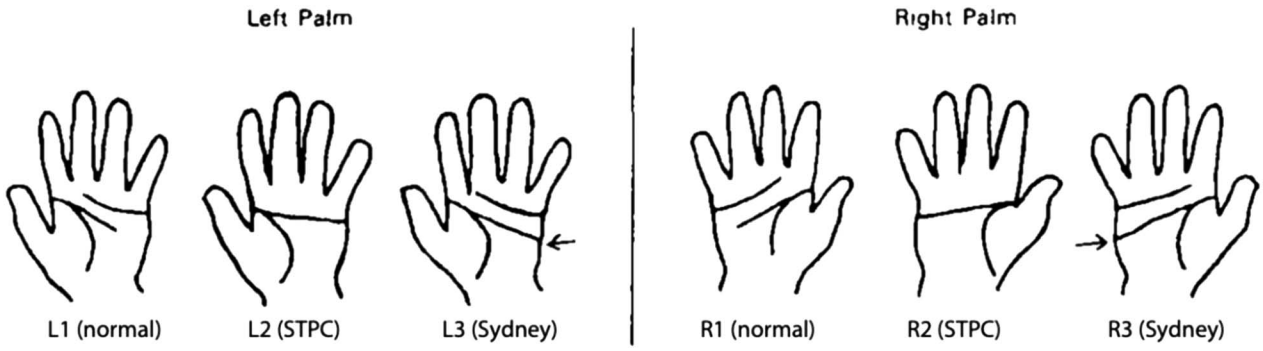
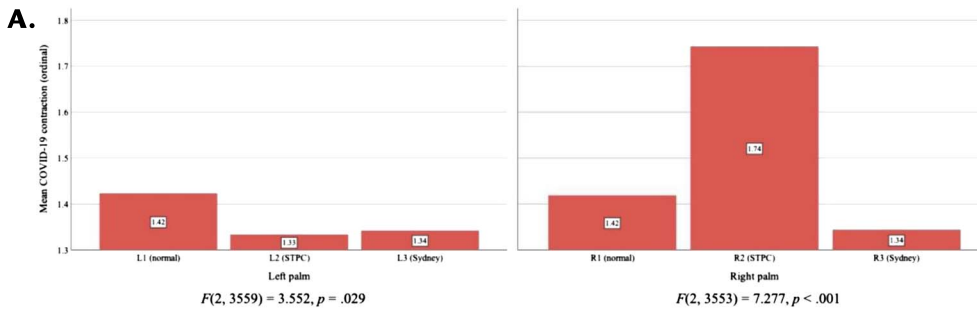


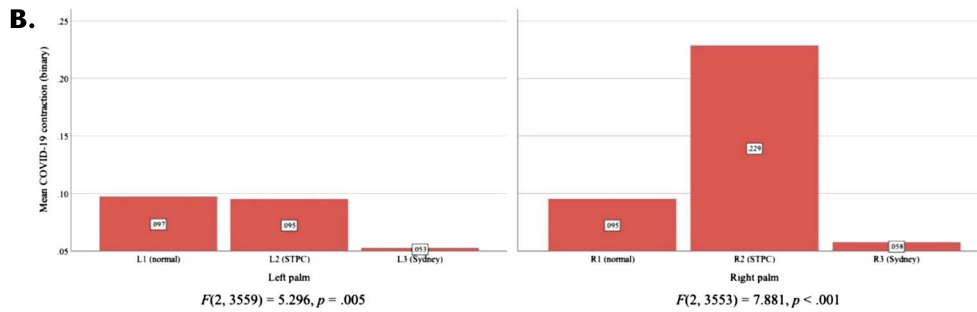
FIGURE 1. Palmar crease types, measured in Sweep 2, BCS (1980), age 10.

n = 8874), and in 2012 (Sweep 8 at age 42; n = 9841). In each sweep, personal interviews were conducted with and questionnaires were administered to the respondents; their mothers, teachers, and doctors during childhood; and their spouses and children in adulthood. Virtually all (96.7%) of the BCS respondents were White. The Centre for Longitudinal Studies of University College London now conducts BCS, and the data are publicly and freely available to registered users of the UK Data Service (https://ukdataservice.ac.uk/).

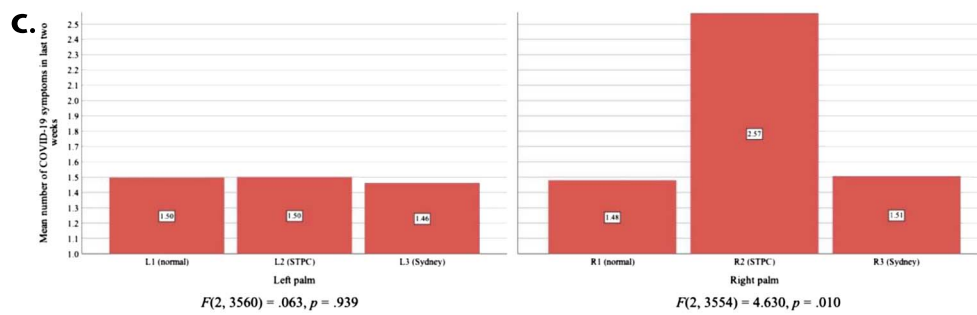
In May 2020, after nearly 2 months of lockdown imposed nationwide by the British government, the Centre for Longitudinal



COVID-19 contraction (ordinal)



COVID-19 contraction (binary)



Number of COVID-19 symptoms

FIGURE 2. Mean COVID-19 susceptibility, by palmar crease type.

Studies contacted all of its respondents and invited them to participate in an online survey designed to collect insights into the lives of the BCS respondents during the lockdown in many facets of their lives: physical and mental health and well-being, family and relationships, education, work, and finances. A large minority (40.4%, n = 4223) of those contacted took part in the online survey. A slightly higher proportion (98.0%) of the May 2020 sample was White. All BCS participants were 50 years old in May 2020. It is important to note that the data were collected long before COVID-19 vaccines were invented, let alone being widely available and administered in 2021.

Dependent Variable: COVID-19 Contraction (Ordinal)

The BCS measured the COVID-19 health status with the question: "Do you think you have or have had coronavirus?"

TABLE 1. Association Between STPC and Sydney Creases With COVID-19 Susceptibility

	Left	**Right**
A. COVID-19 contraction (ordinal)		
Palmar flexion crease		
STPC	−0.380	0.745*
	(0.358)	(0.323)
Sydney	−0.212*	−0.201†
	(0.105)	(0.104)
Threshold		
Y = 1	0.743	0.753
	(0.039)	(0.039)
Y = 2	2.269	2.281
	(0.060)	(0.060)
Y = 3	5.434	5.448
	(0.259)	(0.259)
−2 log likelihood	49.809	53.118
Nagelkerke pseudoR^2	0.002	0.003
No. cases	3562	3556
B. COVID-19 contraction (binary)	**Left**	**Right**
Palmar flexion crease		
STPC	−0.025	1.034*
	(0.529)	(0.407)
	0.975	*2.812*
Sydney	−0.662**	−0.545**
	(0.207)	(0.198)
	0.516	*0.580*
Constant	−2.226	−2.250
	(0.061)	(0.062)
−2 log likelihood	2159.058	2155.379
Nagelkerke pseudoR^2	0.007	0.009
No. cases	3562	3556
C. COVID-19 number of symptoms	**Left**	**Right**
Palmar flexion crease		
STPC	0.002	0.553**
	(0.201)	(0.201)
Sydney	−0.024	0.018
	(0.062)	(0.061)
Constant	0.404	0.391
	(0.024)	(0.024)
Likelihood χ^2	0.152	8.172
No. cases	3563	3557

Main entries are unstandardized regression coefficients.

(Entries in parentheses are standard errors.)

Italicized entries are effects on odds.

"Thresholds" are ordinal regression equivalents of the ordinary least-squares intercept.

†$P < 0.10$.

*$P < 0.05$.

**$P < 0.01$.

The respondent could choose 1 = "no" (67.9%, n = 2868), 2 = "unsure" (23.0%, n = 970), 3 = "yes, based on strong personal suspicion or medical advice" (8.7%, n = 367), or 4 = "yes, confirmed by a positive test" (.4%, n = 18). The author analyzed this variable with ordinal regression.

Dependent Variable: COVID-19 Contraction (Binary)

The author collapsed the original ordinal measure of COVID-19 contraction above into a binary measure: 0 if it is "no" or "unsure" and 1 if it is "yes, based on strong personal suspicion or medical advice" or "yes, confirmed by a positive test." The author analyzed this variable with binary logistic regression.

Dependent Variable: Number of COVID-19 Symptoms

The BCS asked whether the respondent had any of the 18 known symptoms of COVID-19 (fever, cough—dry, cough—mucus or phlegm, sore throat, chest tightness, shortness of breath, runny nose, nasal congestion, sneezing, muscle or body aches, fatigue, unusual loose motions or diarrhea, vomiting, loss of smell, loss of taste, skin rash, headaches, and other) in the last two weeks. The total number of COVID-19 symptoms was a count measure with overdispersion ($M = 1.55$, $s^2 = 4.76$), so the author analyzed it with negative binomial regression.[8]

Independent Variable: Palmar Flexion Creases

At Sweep 2, when the BCS respondents were 10 years old, a physician examined the respondent's left and right palms during the medical examination and noted which of the 3 palmar crease patterns—normal, STPC, or Sydney—the respondent had on the left and the right hand on a form (Fig. 1). The form that the physician filled out did not have the labels for each pattern, which were added by the author. The third variant—Suwon—was not discovered until 2010,[3] 30 years after BCS Sweep 2, and was therefore not included as one of the options.

On the left hand, 83.4% (n = 10,843) had the normal crease, 1.6% (n = 212) had STPC, and 14.9% (n = 1941) had the Sydney crease. On the right hand, 84.4% (n = 10,974) had the normal crease, 1.3% (n = 172) had STPC, and 14.2% (n = 1849) had the Sydney crease.

RESULTS

Figure 2A, left column, shows that the likelihood of early contraction of COVID-19, measured on the ordinal scale, significantly varied by the palmar crease type on the left hand ($F_{2,\ 3599} = 3.552$, $P = 0.029$), and Table 1A, left column, shows that this was because, compared with individuals with the normal crease (reference category), individuals with the Sydney crease were significantly less likely to contract COVID-19 ($b = -0.212$, $P = 0.043$). Figure 2A, right column, shows that the same likelihood also varied significantly by the palmar crease on the right hand ($F_{2,\ 3553} = 7.277$, $P < 0.001$), and Table 1A, right column, shows that this was simultaneously because individuals with STPC were significantly more likely ($b = 0.745$, $P = 0.021$), and those with the Sydney crease were marginally significantly less likely ($b = -0.201$, $P = 0.054$) to contract COVID-19 early.

Figure 2B, left column, shows that the likelihood of early contraction of COVID-19, measured on the binary scale, significantly varied by the palmar crease type on the left hand ($F_{2,\ 3559} = 5.296$, $P = 0.005$), and Table 1B, left column, shows that this was because individuals with the Sydney crease were significantly less likely to contract COVID-19 ($b = -0.662$, $P = 0.001$). Relative to those with the normal crease, the odds of contracting COVID-19 for those with the Sydney crease on the left hand were nearly half ($e^{-0.662} = 0.516$). Figure 2B, right column, shows that the likelihood of early contraction of COVID-19, measured on the binary scale, significantly varied by the palmar crease type on the right hand ($F_{2,\ 3553} = 7.881$, $P < 0.001$). Table 1B, right column, shows that this was because those with STPC were significantly more likely ($b = 1.034$, $P = 0.011$) and those with the Sydney crease were significantly less likely ($b = -0.545$, $P = 0.006$) to contract COVID-19, compared with those with the normal crease. The STPC on the right hand nearly tripled the odds of contraction ($e^{1.034} = 2.812$), and the Sydney crease decreased it by more than 40% ($e^{-0.545} = 0.580$).

Figure 2C, left column, shows that the number of COVID-19 symptoms in the last two weeks did not vary by the palmar crease type on the left hand ($F_{2,\ 3560} = 0.063$, $P = 0.939$), and, accordingly, Table 1C, left column, shows that neither of the coefficients for the palmar crease type was significant (STPC: $b = 0.002$, $P = 0.994$; Sydney: $b = -0.024$, $P = 0.697$). Finally, Figure 2C, right column, shows that the number of COVID-19 symptoms varied significantly with the palmar crease type on the right hand ($F_{2,\ 3544} = 4.630$, $P = 0.010$), and Table 1C, right column, shows that this was because those with STPC had significantly more COVID-19 symptoms ($b = 0.553$, $P = 0.006$).

DISCUSSION

In five of the six comparisons above, the palmar crease type measured in 1980 at age 10 was significantly associated with the contraction of COVID-19 and the number of symptoms suffered among White respondents of the BCS in May 2020 at age 50. Having STPC on the right hand significantly increased the chances of contracting COVID-19 and the number of symptoms suffered, and having the Sydney crease on either hand significantly decreased the chances of COVID-19 contraction. One limitation of the current study is that there were a very small number of confirmed COVID-19 cases in the sample.

Having STPC on the right hand nearly triples the odds of contracting COVID-19 among Whites, and South Asians are 4 to 5 times as likely to have STPC as Whites.[4] This suggests that the genes for and chromosomal abnormalities associated with STPC[6] might potentially be contributing factors to the higher incidence of and mortality from COVID-19 among South Asians in the United Kingdom and elsewhere.[1,2] Because it is extremely easy, quick, and entirely nonintrusive to inspect patients' palms, the findings above from BCS, if replicated, suggest that the inspection of the palmar creases might become part of clinicians' diagnostic and prognostic tools in the fight against COVID-19.

In the May 2020 COVID-19 follow up, BCS asked respondents if they had any of the 16 different long-standing illnesses: cancer; cystic fibrosis; asthma; chronic obstructive pulmonary disease; wheezy bronchitis; diabetes; recurrent backache, prolapsed disc, sciatica, or other back problems; problems with hearing; high blood pressure; heart diseases, congenital or acquired; depression or other emotional, nervous, or psychiatric problems; obesity; chronic obstructive airways disease; infection; HIV/immunodeficiency; and condition affecting the brain and nerves (eg, Parkinson disease, multiple sclerosis). The BCS respondents who had the Sydney palmar crease on their left hand were significantly less likely to suffer from wheezy bronchitis ($t_{2994.000} = 4.134$, $P < 0.001$) and HIV/immunodeficiency ($t_{1333.743} = 2.366$, $P = 0.018$), and those who had the Sydney palmar crease on their right hand were significantly less likely to suffer from chronic obstructive pulmonary disease ($t_{1267.903} = 2.062$, $P = 0.039$), wheezy bronchitis ($t_{2981.000} = 4.134$, $P < 0.001$), and HIV/immunodeficiency ($t_{1383.197} = 2.405$, $P = 0.016$). Thus, combined with the results

for COVID-19 presented above, there seems to be some indication that the genetic and chromosomal abnormalities associated with the Sydney palmar crease might confer some protection against various infectious diseases. Further research is necessary, both to replicate the current findings and to explore the associations between genetic and chromosomal abnormalities associated with nonnormal palmar creases and the propensities toward infectious diseases.

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