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Ischaemic stroke in South Asians: The BRAINS study

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INTRODUCTION

South Asians (Indian, Pakistani, Sri Lankan, Bangladeshi origin) comprise approximately 24% of the world’s population but account for approximately 40% of global stroke deaths [1]. South Asians in the United Kingdom make up the largest ethnic minority group, with over three million individuals [2], and approximately six million in the United States, making them one of the fastest growing immigrant groups in the United States. Much of this large-scale migration, beginning in the 1950s, has resulted in an aging first- and second-generation population who increasingly rely on healthcare resources.

Some small studies have suggested an earlier stroke onset in South Asians and higher stroke mortality regardless of location compared to White populations [3, 4]. Other studies have shown that migration can have an adverse effect on South Asian health due to changes in living environments, differing healthcare systems [5], reduced exercise, and potentially changes in diet [6, 7], possibly compounded by genetic liabilities [8]. Although these negative effects could be reduced by the use of technology to improve healthcare access [9], ethnic-specific analysis is probably needed to identify stroke-onset differences as well as novel risk factors.

We sought to investigate stroke-onset differences between the White British population and South Asians residing in the United Kingdom and in South Asia. We used the UK and India arms of the ongoing international prospective hospital-based BRAINS (Bio-Repository of DNA in Stroke [10, 11]) study, which has recruited patients from 23 secondary healthcare sites in those two countries. To the best of our knowledge, this is the largest comparative ischaemic stroke study to date in South Asians.

MATERIALS AND METHODS

Data source

We analysed the UK and Indian arms of the ongoing prospective international BRAINS study, the details of which have been previously published [10, 11] but are described again here in brief. This hospital-based study meets all ethical standards set by local institutional review boards and has received full institutional ethics approval in the United Kingdom and India. UK stroke patients were screened at 21 participating hospital sites located in London, Sussex, Surrey, West Yorkshire, the West Midlands, Kent, Bedfordshire and Lancashire. The recruitment period was between 2010 and 2019. The sites were chosen to include regions with high South Asian populations while also being representative of the

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Abstract

Background and purpose: Studies on stroke in South Asian populations are sparse. The aim of this study was to compare differences in age of onset of ischaemic stroke in South Asian patients living in the United Kingdom and South Asian patients living in India versus White British stroke patients.

Methods: We studied the UK and Indian arms of the ongoing BRAINS study, an international prospective hospital-based study of South Asian stroke patients. The BRAINS study includes 4038 South Asian and White British patients with first-ever ischaemic stroke, recruited from sites in the United Kingdom and India.

Results: Of the included patients, 1126 were South Asians living in India (ISA), while 1176 were British South Asian (BSA) and 1736 were White British (WB) UK residents. Patients in the ISA and BSA groups experienced stroke 19.5 years and 7.2 years earlier than their WB counterparts, respectively (mean [interquartile range] age: BSA 64.3 [22] years vs. ISA 52.0 [18] years vs. WB 71.5 [19] years; p < 0.001). Patients in the BSA group had higher rates of hypertension, diabetes mellitus and hypercholesterolaemia than those in the ISA and WB groups. After adjustment for traditional stroke risk factors, an earlier age of stroke onset of 18.9 years (p < 0.001) and 8.9 years (p < 0.001) was still observed in the ISA and BSA groups, respectively. In multivariable stepwise linear regression analysis, ethnicity accounted for 24.7% of the variance in early age onset.

Conclusion: Patients in the BSA and ISA groups experienced ischaemic stroke approximately 9 and 19 years earlier, respectively, than their WB counterparts. Ethnicity is an independent predictor of early age of stroke onset. Our study has considerable implications for public health policymakers in countries with sizable South Asian populations.

KEYWORDS
age onset, ethnicity, health inequality, stroke
White British population [12]. The Indian arm screened stroke patients at two hospital sites located in New Delhi (All India Institute of Medical Sciences) and Kerala (Sree Chitra Tirunal Institute for Medical Sciences and Technology). All cases were reviewed by a pre-designated onsite neurologist/stroke physician, with the diagnosis of ischaemic stroke confirmed with computed tomography or magnetic resonance imaging. Stroke cases were subtyped using the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification system [13]. Written informed consent was sought for each included case. For those unable to provide written consent, surrogate consent was taken. Extensive demographic data including age, sex and ethnicity were collected during a nurse-led interview. All participants over 18 years of age at the time of stroke event were considered for the study to ensure a representative sample. Ethnicity was obtained via self-identification. South Asian ethnicity was classified as Indian, Pakistani, Sri Lankan or Bangladeshi origin. White British and White Irish ethnicities were classified as White British. Stroke patients were classified as South Asians living in India (ISA group), South Asians living in the United Kingdom (British South Asian [BSA] group), and White British individuals living in the United Kingdom (WB group). All analyses in this study compared the ISA and BSA groups with WB patients as the reference group.

Risk factors for cases were defined as: hypertension diagnosed at discharge (≥140/90 mmHg), previous diagnosis of hypertension or pre-treatment stage with antihypertensive drugs; hypercholesterolaemia, defined by previous diagnosis or serum cholesterol >5.2 mmol/L; diabetes mellitus, defined as a previous diagnosis of type 1 or 2 diabetes. Previous diagnosis of ischaemic heart disease and atrial fibrillation data were collected from clinical records. Smoking and alcohol history were recorded if the patient smoked or consumed alcohol on a regular basis. Central obesity was defined by large waist circumference (men ≥102 cm, women ≥88 cm) or high body mass index (≥30 kg/m²) [14].

### Standard protocol approvals, registrations and patient consents

A not-for-profit stroke patient support group advised on the original protocol for recruitment of patients. Appropriate ethical approval for this study was obtained in both the United Kingdom and India. The clinical trial registration (http://www.clinicaltrials.gov) unique identifier is: NCT05491824.

### Statistical analysis

Demographic details and categorical data were compared among the ISA, BSA and WB groups using independent t-tests and chi-squared tests. Ages of onset for each TOAST subtype were compared using a one-way analysis of variance (ANOVA) test. General linear model analysis was performed to identify associations between ethnicity and age, adjusted for potential confounders [15]. Variables likely associated with age were selected with respect to biological plausibility (sex, central obesity, smoking history, alcohol history, hypertension, diabetes mellitus, hypercholesterolaemia, ischaemic heart disease and atrial fibrillation). To assess the independent association of age of stroke onset with ethnicity, we conducted a simple linear regression (i.e., the model adjusted for ethnicity and sex only) predicting age of ischaemic stroke (years), adjusting for each traditional stroke risk factor separately. Little's test was used to assess if traditional stroke risk factors with missing values were missing completely at random (MCAR) [16]. A p value < 0.05 was taken to indicate statistical significance. Results were analysed using SPSS v25.0 Statistical Software for Windows.

### RESULTS

The combined UK and India arms of the BRAINS study consist of 6207 patients. Of these, 4038 individuals were identified as having experienced first-time ischaemic stroke, including 1126 (757 men, 369 women) in the ISA group, 1176 (761 men, 415 women) in the BSA group and 1736 (966 men, 770 women) in the WB group. Demographic and clinical characteristics, stratified by ethnicity, are presented in Table 1. The BSA group experienced ischaemic stroke onset 7.2 years earlier and the ISA group 19.5 years earlier than their WB counterparts (mean [interquartile range] age 64.3 [22] years in the BSA group vs. 52.0 [18] years in the ISA group vs. 71.5 [19] years in the WB group; p < 0.001). The BSA group had a greater prevalence of hypertension (BSA 76.9% vs. ISA 68.0% vs. WB 66.3%; p < 0.001), diabetes mellitus (BSA 50.3% vs. ISA 32.9% vs. WB 18.8%; p < 0.001), hypercholesterolaemia (BSA 52.6% vs. ISA 36.4% vs. WB 34.1%; p < 0.001) and ischaemic heart disease (BSA 30.3% vs. ISA 13.6% vs. WB 19.5%; p < 0.001) compared to the ISA and WB groups. Atrial fibrillation, smoking history and high alcohol consumption were more prevalent in the WB group (Table 1).

Sex-specific analyses are presented in Table S1. Men in the ISA group experienced stroke 10.7 years and 17.0 years earlier than men in the BSA and WB groups, respectively, while women in the ISA group experienced stroke 15.5 years and 23.2 years earlier than women in the BSA and WB groups, respectively. With regard to environmental factors, ISA, BSA and WB women reported a greater prevalence of central obesity compared to men. Smoking history and alcohol consumption were greater in men compared to women for each ethnicity. Comparisons of traditional stroke risk factors among the different ethnicities are presented in Table S2. The BSA group had a higher prevalence of small-vessel occlusion (BSA 31.1% vs. ISA 20.0% vs. WB 21.0%; p < 0.001) and a lower prevalence of large-artery atherosclerosis (BSA 19.1% vs. ISA 25.4% vs. WB 33.4%; p < 0.001) and cardio-embolism (BSA 16.2% vs. ISA 11.8% vs. WB 19.8%; p < 0.001) compared to the WB group. However, despite differences in prevalence, patients in the ISA...
group experienced stroke at a younger age across all stroke subtypes compared to their BSA and WB counterparts (Figure 1).

To evaluate the association of age of stroke onset with ethnicity, a linear regression model was used, with adjustment for the following variables: sex, central obesity, alcohol consumption, smoking history, hypertension, atrial fibrillation, and ischaemic heart disease. In a simple linear regression, both the BSA and ISA groups were associated with an earlier age of onset (β = −9.61, SE = 0.27) and accounted for 24.6% of the total variance ($R^2 = 0.246$). A forward stepwise linear regression was performed, adjusting for traditional stroke risk factors (Table 2). In this model, South Asian ethnicity, regardless of location, continued to show a negative association with age of stroke onset (β = −9.31, standard error = 0.31). This model overall predicted 33.7% ($R^2 = 0.337$) of the variation in age of onset of ischaemic stroke, with ethnicity accounting for 24.7% ($R^2 = 0.247$). The results of the missing values analysis (MCAR test) indicated that missing values occurred completely at random ($p = 0.69$).

To assess the independent association of age with ethnicity among stroke patients, the analyses were repeated on the basic model (i.e., the model adjusted for ethnicity and sex only) with separate adjustments for each predictor listed in Table 3. An earlier age of stroke onset was still observed in both the BSA and ISA groups, regardless of the traditional risk factor being adjusted for, suggesting that ethnicity was independently associated with age of stroke onset. After adjustment for these traditional risk factors for stroke, the ISA and BSA groups showed an even more pronounced earlier age of stroke onset of 18.9 years (ISA 52.8 years vs. WB 71.7 years; $p < 0.001$) and 8.9 years (BSA: 62.8 years vs. WB: 71.7 years; $p < 0.001$), respectively.

### DISCUSSION

In this study, compared to their stroke counterparts in the WB group, patients in the BSA and ISA groups had an earlier ischaemic stroke onset of approximately 9 and 19 years, respectively, following adjustment for traditional stroke risk factors. In both men and women, the ISA group still had an earlier ischaemic stroke onset compared to the BSA and WB groups. For each stroke subtype (including the commonest subtype small-vessel occlusion), patients in the ISA group continued to exhibit a significantly earlier age of onset compared to their WB counterparts. Ethnicity explained approximately 25% of the variance in age of onset, with the traditional risk factors of hypertension, atrial fibrillation, ischaemic heart disease, alcohol consumption, central obesity, and sex accounting for only approximately 8% of the variance.

The significantly later age of onset of ischaemic stroke in the BSA group compared to the ISA group suggests an improvement in stroke prevention associated with the UK environment [17]. Our study is the first migration-related study focusing on age of first onset of ischaemic stroke among South Asians in the United Kingdom and India [18], which limits comparisons with previous studies. Earlier age of stroke onset in South Asians, regardless of

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**Table 1** Population characteristics stratified by ethnicity

<table>
<thead>
<tr>
<th></th>
<th>ISA group</th>
<th>BSA group</th>
<th>WB group</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 1126)</td>
<td>(n = 1176)</td>
<td>(n = 1736)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (IQR) age of onset, years</td>
<td>52.0 (18)</td>
<td>64.3 (22)</td>
<td>71.5 (19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>757 (67.2)</td>
<td>761 (64.7)</td>
<td>966 (55.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TOAST stroke subtype, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large-artery atherosclerosis</td>
<td>216 (25.4)</td>
<td>185 (19.1)</td>
<td>414 (33.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Small-vessel occlusion</td>
<td>170 (20.0)</td>
<td>302 (31.1)</td>
<td>261 (21.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>100 (11.8)</td>
<td>157 (16.2)</td>
<td>246 (19.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Environmental factors, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central obesity</td>
<td>348 (35.8)</td>
<td>358 (35.0)</td>
<td>368 (31.1)</td>
<td>0.042</td>
</tr>
<tr>
<td>Smoking history</td>
<td>492 (43.9)</td>
<td>413 (35.5)</td>
<td>915 (53.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>468 (41.8)</td>
<td>254 (23.2)</td>
<td>660 (45.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>747 (68.0)</td>
<td>890 (76.9)</td>
<td>1137 (66.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>361 (32.9)</td>
<td>582 (50.3)</td>
<td>321 (18.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>355 (36.4)</td>
<td>593 (52.6)</td>
<td>579 (34.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>147 (13.6)</td>
<td>340 (30.3)</td>
<td>300 (19.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>56 (6.1)</td>
<td>131 (11.7)</td>
<td>372 (21.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: $n$, sample size. Central obesity was defined by waist circumference (men >102 cm, women >88 cm) or body mass index ($\geq 30$ kg/m$^2$). An independent t-test was used to compare age of onset with all other comparisons using chi-squared test. Stroke subtype was defined using the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification system.

Abbreviations: BSA, British South Asians living in the United Kingdom; IQR, interquartile range; ISA, South Asians living in India; WB, White British individuals living in the United Kingdom.
location, is consistent with findings from other smaller studies, both in South Asia [1, 19–21] and the United Kingdom [22], although these do not focus on first-time stroke events. Notwithstanding the health benefits of living in the United Kingdom, the BSA population has not standardized to the WB population, although findings in the BSA group were better compared with the ISA group. Gunarathne
et al. found an 8-year earlier stroke onset in BSA compared to WB patients, with data collected between 1997 and 2005 [22], suggesting that little improvement in stroke prevention has been achieved in this migrant demographic over the intervening decades.

This study is also the first to report age of event for each stroke subtype in the South Asian demographic. Patients in the ISA group consistently experienced earlier stroke onset than their BSA and WB counterparts regardless of TOAST classification. We also report stark differences in the prevalence of stroke subtypes, with that of small-vessel occlusion being approximately 1.5-fold higher in the BSA group compared to the WB population. A possible reason for this age discrepancy may be the higher prevalence of traditional risk factors in the BSA patients [4, 23–26]. We report significantly higher rates of hypertension, diabetes mellitus and hypercholesterolaemia in BSA patients, consistent with some [4, 25–31] but not all previous studies [29]. After adjusting for these risk factors, South Asian ethnicity explained 24.7% of the earlier stroke onset seen in this study and this ethnicity was associated with an earlier age of onset of stroke. Appropriate clinical management of these comorbidities may also play a part in determining age of stroke onset [32, 33].

Central obesity (a known ischaemic stroke risk factor) has a greater prevalence among the South Asian community [34–36]. Although our study found a significantly higher prevalence of central obesity in the BSA group, a similar prevalence in the ISA group when compared to the WB group was also present. This highlights the possible changes in lifestyle/environmental factors associated with migrating to the United Kingdom such as diet and exercise. The traditional South Asian diet consisting of carbohydrate-rich foods including rice and bread is more tailored to a physically demanding rural environment [37]. However, this carbohydrate-rich diet continues among South Asian people in the United Kingdom [38], partnered with lower physical activity compared with the WB population [6, 39, 40]. A predisposition to visceral adiposity in the truncal region has resulted in the World Health Organization recommending South Asian-specific thresholds for determinants of obesity [41].

Although an increased prevalence of traditional stroke risk factors in South Asians was seen in both the United Kingdom and India, the effect of migration on environmental and lifestyle factors is another possible cause for differing stroke risks and outcomes. Accessing healthcare is an important area in stroke prevention which is often overlooked in migration studies. Although the BSA population has access to preventative healthcare services, knowledge about risk factors and contribution to disease is also demonstrably poor. Many BSA patients are not aware of the common complications associated with diabetes mellitus, the importance of screening clinics and the need to engage with chiropodists [42]. Furthermore, sociocultural and religious factors can exaggerate this decreased awareness with the distorted perceptions of failure at self-care and social stigma [43]. Sex differences can also determine environmental and comorbidity factor prevalence. Of interest was the approximately 10% higher prevalence of ischaemic heart disease among BSA men compared to women. In general, ischaemic heart disease is more likely to develop at an earlier age in men [44], who usually have a greater prevalence of cardiovascular risk factors, which is the likely reason for the difference.

In common with the previous literature, stroke of undetermined aetiology was the most common TOAST subtype in the ISA group [45, 46]. To be considered as small-vessel occlusion the lesion diameter is required to be <15 mm. Furthermore, to be considered to have large-artery atherosclerosis, patients are required to have stenosis of >50%. If either of these criteria are not met, then patients with mild stenosis or those with small-vessel occlusion but large lesion

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>ISA (WB reference group)</th>
<th>BSA (WB reference group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect size (β), years SE p value</td>
<td>Effect size (β), years SE p value</td>
<td></td>
</tr>
<tr>
<td>Central obesity</td>
<td>−19.60 0.56 &lt;0.001</td>
<td>−13.29 0.54 &lt;0.001</td>
</tr>
<tr>
<td>Smoking history</td>
<td>−19.29 0.52 &lt;0.001</td>
<td>−13.26 0.48 &lt;0.001</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>−19.36 0.54 &lt;0.001</td>
<td>−13.69 0.50 &lt;0.001</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>−19.37 0.50 &lt;0.001</td>
<td>−13.50 0.45 &lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>−19.63 0.52 &lt;0.001</td>
<td>−13.92 0.48 &lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>−19.12 0.54 &lt;0.001</td>
<td>−12.90 0.48 &lt;0.001</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>−18.94 0.55 &lt;0.001</td>
<td>−13.25 0.48 &lt;0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>−18.27 0.55 &lt;0.001</td>
<td>−11.59 0.48 &lt;0.001</td>
</tr>
<tr>
<td>Multivariate model</td>
<td>−18.77 0.65 &lt;0.001</td>
<td>−13.88 0.58 &lt;0.001</td>
</tr>
</tbody>
</table>

Note: Effect size (β-coefficients), degree of change in age of onset of ischaemic stroke (dependent variable) for every 1-unit change in the predictor variable. Each model was adjusted for sex and specific stroke risk factor. Multivariate model includes all risk factors.

Abbreviations: BSA, British South Asians living in the United Kingdom; ISA, South Asians living in India; SE, standard error; WB, White British individuals living in the United Kingdom.
size will be classified as having stroke of undetermined aetiology [47].

As with all studies, several limitations of this study should be noted. The BRAINS study is a long-running study and thresholds for risk factors and their management have changed over the intervening years. However, such transitions would have resulted in a non-differential ethnic bias and are not likely to have affected the significance of the results in this study. Comorbidity prevalence is recorded at the time of the event. Although we are unable to comment on the length of time these comorbidities were present prior the stroke event, many of the prevalence data were collected through treatment regimens recorded on the patient’s clinical record. Although this may lead to an underestimation of the real effect size on the age of stroke event of the included stroke risk variables, our large sample size (n = 4038) reflects the current impact of these risk variables on stroke in the South Asian population. Ethnicity was defined by grandparent origin. Despite this being self-reported, previous studies have demonstrated the accuracy of this methodology [48, 49]. Data on socioeconomic status, which may influence morbidity and mortality, were not collected so we were unable to assess its influence on age of stroke onset. This was a prospective hospital-based study so conclusions cannot be extrapolated for overall or community-based age differences. Furthermore, older stroke patients may choose not to seek medical advice compared to younger patients, which could influence this hospital-based study. However, it is likely that this limitation would apply to either ethnic group or location. Although we did not collect detailed data on the numbers of those who chose not to participate in this prospective study, those numbers were small and broadly similar across all studied groups. To assess the representativeness of the ISA and BSA groups within our study we used the broader BRAINS dataset, which consists of both ischaemic and haemorrhagic events, and found similar stroke subtype prevalence across the three groups included in our study [4, 17]. This includes BSA patients in the BRAINS study reporting 84.5% of ischaemic events, which is similar to previous reported prevalence [4]. Further, we were unable to report specific effects of migration and how they have developed because long-term follow-up was not undertaken.

Both the UK and India recruitment sites were chosen to ensure a representative sample. In the United Kingdom we identified 21 hospital sites with a high number of South Asian patients. In India, with its geographical land mass similar to that of the United States, it is significantly more challenging to recruit a representative sample. The two hospital sites chosen, the All India Institute of Medical Sciences and the Sree Chitra Tirunal Institute for Medical Sciences and Technology, were identified as they are located in the north and south of the country. Furthermore, both offer free access to medical services and thus are more likely to attract a wide population from varying socioeconomic backgrounds. Finally, this was a hospital-based study and was dependent on recruitment of patients attending hospital. Populations with different cultures have different attitudes towards seeking and different access to emergency healthcare. While stroke usually presents with disabling symptoms, not all afflicted patients attend hospital, which could lead to recruitment bias.

In conclusion, patients in the BSA and ISA groups experienced stroke approximately 9 and 19 years earlier, respectively, than their WB counterparts. Ethnicity accounted for approximately 25% of the variance in early age of onset. Our work has considerable implications for public health policymakers in countries with sizable South Asian populations.

**AUTHOR CONTRIBUTIONS**

Pankaj Sharma conceived and overall directed the global BRAINS study. Kameshwar Pasad was the lead investigator in India. Taylor Aurelius undertook the analysis and wrote the first draft. Taylor Aurelius, Gie Ken-Dror and Pankaj Sharma undertook the analysis. Sapna D. Sharma assisted with clinical phenotyping. Ankita Maheshwari, Sageet Amrani, Gunaratnam Gunathilagan, David L. Cohen, Chakravarthi Rajkumar, Stuart Maguire, Sissi Isopoglou, Ibrahim Balogun, Anthea Parry, Lakshmanan Sekaran, Hafiz Syed, Enas Lawrence, Ravneeta Singh, Ahamad Hassan, Chris Wharton, Khalid Javald, Neetish Goorah, Peter Carr, Eman Abdus Sami, Shri Ram Sharma, Padmavathy N. Sylaja, Kameshwar Pasad and Pankaj Sharma contributed to collection of data. All the authors contributed to the final draft. Pankaj Sharma accepts overall responsibility for the final work.

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**CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**ETHICAL APPROVAL**

Appropriate ethical approval for this study was obtained in both the United Kingdom and India (Riverside Research Ethics Committee: 04/Q0401/40).

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**SUPPORTING INFORMATION**

Additional supporting information can be found online in the Supporting Information section at the end of this article.