Incidence of clinically suspected venous thromboembolism in British Indian patients

BM Siddiqui, MS Patel, S Rudge, A Best, J Mangwani

University Hospitals of Leicester NHS Trust, UK

ABSTRACT

INTRODUCTION Venous thromboembolism (VTE) remains a major public health issue around the world. Ethnicity is known to alter the incidence of VTE. To our knowledge, there are no reports in the literature investigating the incidence of VTE in British Indians. The aim of this study was to investigate the rates of symptomatic VTE in British Indian patients in the UK.

METHODS Patients referred to our institution between January 2011 and August 2013 with clinically suspected VTE were eligible for inclusion in the study. Those not of British Indian or Caucasian ethnicity were excluded. A retrospective review of these two cohorts was conducted.

RESULTS Overall, 15,529 cases were referred to our institution for suspected VTE. This included 1,498 individuals of British Indian ethnicity. Of these, 182 (12%) had confirmed VTE episodes. A further 13,159 of the patients with suspected VTE were coded as Caucasian, including 2,412 (16%) who had confirmed VTE events. VTE rates were a third lower in British Indians with clinically suspected VTE than in the equivalent Caucasian group. The British Indian cohort presented with VTE at a much earlier age than Caucasians (mean 57.0 vs 68.0 years).

CONCLUSIONS This study suggests that British Indian patients have a lower incidence of VTE and are more likely to present at an earlier age than Caucasians. There was no significant difference in VTE type (deep vein thrombosis vs pulmonary embolism) among the ethnic groups. Clinicians should be aware of variations within ethnicities but should continue to adhere to existing VTE prevention guidance.

KEYWORDS

Venous thromboembolism – Ethnicity – Deep vein thrombosis – Environmental (risk) factors – Pulmonary embolism

Accepted 25 January 2018

CORRESPONDENCE TO

Bobby Siddiqui, E: bobby.siddiqui@gmail.com

Venous thromboembolism (VTE) encompasses two clinically distinct entities: deep vein thrombosis (DVT) and pulmonary embolism (PE). Incidence rates in the UK have been documented as 1–2 per 1,000¹ and they have been attributed as the cause of many thousands of deaths.² Approximately 5–10% of inpatient mortality has been shown to be VTE related.³ The financial implications of diagnosis, treatment, hospitalisation and long-term care impart a significant burden on the National Health Service (NHS).² National programmes have led to VTE prevention becoming firmly embedded in the NHS, with VTE related data collected locally and submitted nationally.

Risk factors for the development of VTE have been documented in the literature.⁴ Evidence suggests that there is a higher incidence of VTE in Black populations than in White and Asian populations^{5–9} but ethnic cohorts were often grouped together, which has led to ambiguity in the interpretation of results. Moreover, definitions of ‘Asian’ ethnicity (specifically in the American literature) encompass nations as diverse as China, Japan, India and

Pakistan.¹⁰ In the UK, those declaring themselves to be ‘Asian’ (ethnicity codes H, J, K and L in Fig 1) originate from the Indian subcontinent and its environs, and are coded in our health system accordingly.¹¹ The term ‘Asian’ has been replaced with ‘British Indian’ for the purposes of this study.

Guidelines issued by the National Institute for Health and Clinical Excellence (NICE) in 2010 form the basis for risk assessment, diagnosis and treatment of patients with VTE in the UK.² Ethnicity is not considered a risk factor for VTE in this guidance. In recent years, studies outside the UK have suggested that Asian ethnicity does not lead to lower risk of VTE.^{12–14} The objective of our study was to investigate the influence of British Indian ethnicity on the incidence of clinically suspected VTE in the UK.

Methods

This study was conducted at University Hospitals of Leicester (UHL) NHS Trust, which is situated in the East

<i>White</i>	
A	British
B	Irish
C	Any other White background
<i>Mixed</i>	
D	White and Black Caribbean
E	White and Black African
F	White and Asian
G	Any other mixed background
<i>Asian or Asian British</i>	
H	Indian
J	Pakistani
K	Bangladeshi
L	Any other Asian background
<i>Black or Black British</i>	
M	Caribbean
N	African
P	Any other Black background
<i>Other ethnic groups</i>	
R	Chinese
S	Any other ethnic group
Z	Not stated

Figure 1 National codes for ethnicity¹¹

Midlands region of England and serves one of the most diverse areas of the UK. Data from the 2011 census show that the City of Leicester has one of the highest proportions of British Indians in the country (28.3%).¹⁵

All patients referred to UHL for imaging to detect the presence of clinically suspected VTE between January 2011 and August 2013 (inclusive) were entered prospectively into a trust-wide encrypted database. A retrospective analysis of these prospectively collected data was carried out. Sources of referral included the emergency department, direct referrals from primary care, outpatient clinics and current inpatients. Data points captured included patient demographics, type of VTE suspected, and modality of imaging requested and subsequent results. Ethnicity was recorded using category codes (Fig 1).¹¹

All patients not classified as White or British Indian and those of mixed ethnicity were excluded, as were individuals with a previous history of VTE (detected through duplicate patient ID numbers). Patients from the two ethnic groups included in the study were categorised either as inpatients or as being referred from outside the hospital.

Deaths following positive VTE imaging were assumed to be related to VTE if occurring within 21 days of VTE diagnosis.

Statistical analysis was conducted using SPSS® version 21 (IBM, New York, US). A *p*-value of ≤0.05 was considered statistically significant.

Results

During the study period, 18,749 people were referred with a clinically suspected episode of VTE. Among these, there were 3,220 duplicate entries, leaving 15,529 cases. Application of exclusion criteria removed another 872 patients. This left 14,657 patients for further analysis (Fig 2). Ten

Figure 2 Flowchart of patient selection

per cent of these (*n*=1,498) were British Indian and ninety per cent (*n*=13,159) were Caucasian.

The overall incidence of symptomatic VTE (irrespective of ethnicity) was 3.39 per 1,000. This represents an average of 1,287 cases per year over the 31-month study period. The symptomatic VTE incidence in the British Indian group was 0.87 per 1,000 while in the Caucasian cohort, it was 4.13 per 1,000. There were 182 confirmed VTE cases among the British Indian patients (12.15%) while the Caucasians had 3,001 confirmed cases (22.81%). Tables 1 and 2 summarise the positive VTE events in the two ethnic groups. There was a significant difference in overall VTE rates (*p*<0.005) but there was no difference in the incidence of type of VTE (DVT or PE) (*p*=0.174).

The age at the time of diagnosis of VTE was also significantly different between the two ethnic cohorts (*p*<0.05). British Indian patients were diagnosed at a mean age of 56.95 years (standard deviation [SD]: 18.26 years, standard error of the mean [SEM]: 2.017) while their Caucasian counterparts were diagnosed at a mean age of 67.95 years (SD: 17.01 years, SEM: 0.466).

In the British Indian group, 33 patients had a recorded death following a VTE diagnosis; 6 (18.2%) of these deaths occurred within 21 days of the diagnosis. Among the Caucasians, 701 patients died following a VTE diagnosis, with 146 deaths (20.8%) occurring within 21 days of imaging results. This difference did not achieve statistical significance (*p*=0.2).

Discussion

There remains a general lack of data examining the influence of ethnicity on the development of VTE. This study is the first to quantify clinically suspected VTE rates in British Indian patients.

Table 1 Positive venous thromboembolism events in British Indian patients

Referral type	Mean age in years (range)	Deep vein thrombosis	Pulmonary embolism
Inpatient (<i>n</i> =75)	57.6 (18.2–88.5)	34	42
Outpatient (<i>n</i> =107)	51.7 (18.1–88.0)	93	14
Total		127	56

Table 2 Positive venous thromboembolism events in Caucasian patients

Referral type	Mean age in years (range)	Deep vein thrombosis	Pulmonary embolism
Inpatient (<i>n</i> =1,250)	69.2 (17.1–101.2)	428	822
Outpatient (<i>n</i> =1,751)	62.9 (17.2–99.5)	1,517	234
Total		1,945	1,056

Previous studies have postulated that genetic, cultural and socioeconomic factors could play a role in VTE development. Lower rates of factor V Leiden and prothrombin G20210A polymorphisms,^{9,16,17} massage, passive exercises, and diets low in fat and meat derived products have been implicated in supposed lower rates of VTE in Asian patients in the past.¹⁵ Nevertheless, current guidelines from the Asian Venous Thrombosis Forum issued to countries of Asia state that all individuals admitted to hospital (irrespective of ethnicity) should have VTE prophylaxis measures instituted.¹⁸

Recent improvements in economic status have led to better access to diagnostic medicine. VTE rates have been increasing steadily to an overall incidence over a 9-year period of 17.46 VTEs per 100,000 admissions.¹² Alongside these advances and the adoption of Western cultures comes the increase in a diet rich in processed, sugar laden, meat derived products. This has most likely contributed significantly to the spreading global epidemic of obesity and may have raised VTE incidence further.⁷

Having had access to better diagnostic healthcare coupled with a presumed 'poor' diet, it could be expected that Asian migrants to the UK may be at an increased risk of a VTE diagnosis¹ but this was not borne out in our study. Incidence of symptomatic VTE was much lower in British Indians than the national average and also when compared with a similar Caucasian group. The investigation for VTE was positive in 12% of the British Indian patients while 25% of the Caucasian cohort had positive imaging. This difference was statistically significant ($p<0.005$).

Rezende *et al* examined data from the MEGA (Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis) study in the Netherlands.¹⁴ They concluded that East/Southeast Asian immigrants had the lowest rates of VTE in their study population, even when adjusting for several environmental and genetic factors. There was no difference in terms of VTE rates between first and second generation immigrants. This adds to

existing evidence against cultural 'acclimatisation', which immigrants may acquire during their stay in a host nation.¹⁹ It also suggests that genetic influences are stronger than cultural influences in the development of symptomatic VTE.

Liao *et al* found similar ethnic differences in their New Zealand study.¹⁷ Patients of Indian heritage had an approximately sixfold reduction in VTE rates compared with those of European descent. Their study population was comparable with ours in that there was high ethnic diversity in a similar sized, Western society.

Those with positive VTE imaging in the British Indian group were on average at least ten years younger than their Caucasian counterparts. Wang *et al* found the mean age at VTE diagnosis in a Chinese population to be 58.8 years,²⁰ very similar to our finding of 57.0 years in Indian patients. It could therefore be argued that age should carry more weight when risk assessing Indian patients, given the well documented association of VTE and age.⁴ NICE guidance lists age ≥ 60 years as a risk factor for VTE development² but does not take ethnicity into account.

Irrespective of ethnicity, there was a tendency for DVT to account for the majority of VTE episodes in cases referred from outside our institution but this pattern was reversed when considering inpatient referrals. This has been well noted in previous studies, including other ethnicity studies.¹⁴ We were, however, unable to detect a statistically significant difference in type of VTE (DVT or PE) between the ethnic groups in the present study.

Our study has incorporated a large volume of data, collected prospectively and updated in real time from multiple hospital departments, all from a region of high cultural diversity. As a result, a large enough sample size was obtained without needing to collate different ethnicities to achieve statistical significance. This study offers further evidence to the small number of UK-based studies and as such, the data are likely to be more applicable to the whole NHS.

Study limitations

Limitations of this study include non-availability of comprehensive data on the presence of risk factors and incomplete recording of medical co-morbidities. This could have influenced our results. In addition, although mortality following VTE episodes was recorded, it was not possible to see which of these deaths were directly attributable to the index VTE episode.

Assumptions had to be made regarding duplicate entries. It was felt that all duplicate entries indicated a history of previous VTE (a known major risk factor) or previous referral to our trust on the grounds of suspected VTE. For this reason, these cases were excluded from our analysis.

A further assumption was made concerning first time presentations (ie patients with no previous hospital attendances and co-morbidities). It was presumed that these individuals were otherwise fit and well, and that VTE occurred spontaneously.

It is recognised that there are also diagnostic challenges and that referrals were only made for symptomatic cases. This means our study could have missed those patients who may have incidental or asymptomatic diagnoses.

Future work

Differentiation of VTE risks between first, second or even third generation immigrants should be made in future studies. The role of ethnicity in tandem with other known risk factors (such as orthopaedic surgery or lower limb cast immobilisation) would form the basis of future publications from our institution.

The clinical benefit of chemical prophylaxis in British Indian patients must be reviewed to ensure that this group is not exposed to unnecessary risks of bleeding. Furthermore, there remains the potential of significant financial savings if chemical/mechanical prophylaxis can be safely omitted.

Conclusions

This study has highlighted that VTE rates in clinically suspected cases are significantly lower in British Indians than the national average and that they present with VTE at a much younger age than Caucasians. Despite the lower rates, altering current treatment guidelines is not recommended.

It should be at the forefront of the clinician's mind that a British Indian ethnic background strongly influences the

development of VTE. Age should carry more weight when risk assessing patients of British Indian ethnicity.

References

1. NHS England. *Commissioning Services that Deliver High Quality VTE Prevention: Guidance for Commissioners*. London: NHS England; 2013.
2. National Institute for Health and Clinical Excellence. *Venous Thromboembolism: Reducing the Risk for Patients in Hospital*. London: NICE; 2010.
3. Cohen AT, Tapson VF, Bergmann JF *et al*. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. *Lancet* 2008; **371**: 387–394.
4. Anderson FA, Spencer FA. Risk factors for venous thromboembolism. *Circulation* 2003; **107**: 19–116.
5. White RH, Zhou H, Romano PS. Incidence of idiopathic deep venous thrombosis and secondary thromboembolism among ethnic groups in California. *Ann Intern Med* 1998; **128**: 737–740.
6. Bagaria V, Modi N, Panghate A, Vaidya S. Incidence and risk factors for development of venous thromboembolism in Indian patients undergoing major orthopaedic surgery: results of a prospective study. *Postgrad Med J* 2006; **82**: 136–139.
7. White RH, Keenan CR. Effects of race and ethnicity on the incidence of venous thromboembolism. *Thromb Res* 2009; **123**(Suppl 4): S11–S17.
8. Roberts LN, Patel RK, Arya R. Venous thromboembolism and ethnicity. *Br J Haematol* 2009; **146**: 369–383.
9. Zakai NA, McClure LA. Racial differences in venous thromboembolism. *J Thromb Haemost* 2011; **9**: 1,877–1,882.
10. Klatsky AL, Baer D. What protects Asians from venous thromboembolism? *Am J Med* 2004; **116**: 493–495.
11. NHS Data Model and Dictionary. Ethnic category code. http://www.datadictionary.nhs.uk/data_dictionary/attributes/e/end/ethnic_category_code_de.asp (cited February 2018).
12. Lee AD, Stephen E, Agarwal S, Premkumar P. Venous thrombo-embolism in India. *Eur J Vasc Endovasc Surg* 2009; **37**: 482–485.
13. Angral R, Islam MS, Kundan S. Incidence of deep vein thrombosis and justification of chemoprophylaxis in Indian patients: a prospective study. *Bangladesh Med Res Counc Bull* 2012; **38**: 67–71.
14. Rezende SM, Lijfering WM, Rosendaal FR, Cannegieter SC. The risk of venous thrombosis in different immigrant groups in the Netherlands. *Blood* 2012; **120**: 3393.
15. BBC News. Census 2011: Leicester 'most ethnically diverse' in region. <https://www.bbc.co.uk/news/uk-england-leicestershire-20678326> (cited February 2018).
16. Angchaisuksiri P. Venous thromboembolism in Asia – an unrecognised and under-treated problem? *Thromb Haemost* 2011; **106**: 585–590.
17. Liao S, Woulfe T, Hyder S *et al*. Incidence of venous thromboembolism in different ethnic groups: a regional direct comparison study. *J Thromb Haemost* 2014; **12**: 214–219.
18. Liew NC, Chang YH, Choi G *et al*. Asian venous thromboembolism guidelines: prevention of venous thromboembolism. *Int Angiol* 2012; **31**: 501–516.
19. Klatsky AL, Armstrong MA, Poggi J. Risk of pulmonary embolism and/or deep venous thrombosis in Asian-Americans. *Am J Cardiol* 2000; **85**: 1,334–1,337.
20. Wang H, Ye J, Wang L, Jin W. Risk characteristics of venous thromboembolism in Chinese patients. *Clin Appl Thromb Hemost* 2016; **22**: 490–494.