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Assessing thromboembolic disease burden, risk perception, management, and management outcomes in Ghana

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ABSTRACT

Despite the widely documented and economic burden of thromboembolic disease (TED) globally, data on the true impact of the disease in Ghana are scanty. This study, therefore, aimed to assess TED burden, risk perception, and thromboprophylactic practices across general medical, surgery, and obstetrics and gynecology specializations in Ghana. A quantitative cross-sectional study was conducted in tertiary regional/district, polyclinic, and private hospitals in the Kumasi Metropolis of the Ashanti region of Ghana. The study indicated that TED was classified as medium risk in most areas of clinical practice and mostly reported in inpatient settings. Deep vein thrombosis and ischemic stroke were the most commonly reported diseases, with pain being the most common symptom. The practice of thromboprophylaxis was averagely practiced in most areas of clinical practice. Pharmacological management of TED was preferred with low-molecular-weight heparins and warfarin being the most widely used therapeutic options. The cost was the greatest factor hindering therapy and choice of medication. Bleeding was the most common side effect observed with therapy. Although therapies for management and prophylaxis of TED are available and effective, it is still a burden and perceived as a risk in clinical practice and healthcare delivery in Ghana because of the high cost of therapy.

INTRODUCTION

Thromboembolic disease (TED) are circulatory system disorders that involve blood clots within a blood vessel and plugging of blood vessels (Goldhaber, 2005). TED consist of both venous and arterials thromboembolic events (VTE and ATE). Deep vein thrombosis (DVT) and pulmonary embolism (PE) are two prominent venous diseases (TED) (Goldhaber, 2005). ATE are a common pathology underlying several cardiovascular diseases such as ischemic heart disease (acute coronary syndromes), peripheral arterial disease, and ischemic stroke (IS) (Yuxiang and Junbo, 2012). DVT and PE are predominantly a disease of the elderly, with a low annual incidence of 1 in 100,000 in populations less than 45 years of age, and this incidence sharply rises to 5–6 in 1,000 in adult populations 80 years and above, probably due to the presence of comorbidities,for example, like diabetes, and also an increase in coagulation potential (Cushman, 2007).

Despite the wealth of research data on the incidence, burden, and management of thromboembolic disorders in the world, similar data from sub-Saharan countries, such as Ghana, remain very scanty. Such data will go a long way in improving disease knowledge and awareness, informing policy direction in terms of resources, and improving standards in healthcare delivery across the country.

This study, therefore, assessed the TED burden, risk perception, and thromboprophylaxis practices across different healthcare specializations, i.e., general practice (GP), medicine, surgery, and obstetrics and gynecology in the Kumasi Metropolis of the Ashanti region of Ghana. It assessed current therapeutic management, with the possible recommendation of herbal medicines, by health practitioners, as well as limitations and factors influencing the choice of therapy in the orthodox healthcare setting.

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MATERIALS AND METHODS

Study area

This study was carried out in the cosmopolitan city of Kumasi, the administrative capital of the Ashanti region. Kumasi has a population of 1.73 million people and covers an area of 254 km^2, according to the 2010 population and housing census (PHC, 2010). The Ashanti region, for that matter Kumasi, is strategically located. This makes it accessible to people from both the northern parts of the country and coastal belts. It also has a unique blend of people from all parts of the country; these make it an ideal study area. Kumasi has a proportionate distribution of different types of healthcare facilities (private, polyclinic, regional, and teaching hospitals) manned by abled health practitioners offering different types of specialized healthcare services, i.e., surgical, medical, GP, and obstetrics and gynecology. Data thus gathered from this study will be seemingly representative of the entire country because of these unique characteristics Kumasi offers.

Study setting

The study was carried out in a multicenter setting across 10 different healthcare institutions which included one tertiary institution of teaching hospital status, one public institution of district/regional hospital status, three public institutions of polyclinic status, and five private hospitals.

Study population

The study population was healthcare practitioners, i.e., doctors, nurses, and pharmacists drawn from research institutions in the study setting. These categories of healthcare professionals were selected because focus was on those directly involved in patient care and pharmacological management and monitoring.

Inclusion and exclusion criteria

Sampled health practitioners were considered eligible for this study if

- they worked in an institution that offered both in-patient and out-patient services and recorded at least on average 30 old cases and five new cases daily;
- they were directly involved in the management of patients who might present with TED, that is, prescription of medications, drug administration, patient monitoring, and/or medication counseling in the past 12 months.

Health practitioners who did not meet these criteria were excluded from this study.

Sample size determination

Yamane's sample size formula is as follows: $n = N/1+Ne^2$, where n is the sample size, the N the desired population of interest, and e is the acceptable sampling error (usually at 5% or 0.05) (Yamane, 1967).

Therefore, at a population of interest of 150 healthcare professionals in the Kumasi cosmopolitan area ($n = 150$),

$$n = 150/1 + 150(0.05)^2 = 109.$$

Therefore, a sample size of 109 professionals was used for the study.

Sampling technique

A sample size of 109 professionals was randomly selected across selected institutions.

Data collection tool

A questionnaire written in English with four Sections A–D was designed in this study since all healthcare providers involved in the study were trained using the English language. covered socio-demographics of respondents, Section B covered the prevalence of TED and risk perception among health professionals, Section C covered the practice of thromboprophylaxis and management outcomes, and Section D covered the possible use of herbal medicines in the management and prophylaxis of TED. The questionnaire consisted of questions with multiple-choice answers for respondents to tick the appropriate response. Some questions had the option of multiple answers, with others also giving room for a free text response to be written when necessary.

The questionnaire was pretested by the administration to five respondents in each category of healthcare professionals to validate and ensure that questions could capture relevant information needed for this study.

Study design and data collection

This study was a quantitative study that employed a cross-sectional design in a survey. It is also a descriptive survey because it is designed to measure certain phenomena in a population of interest at a point in time. This descriptive cross-sectional study deemed appropriate in arriving at the desired outcome or objectives of this research was conducted between October 2017 and November 2017 over a 5-weeks period. A pretest questionnaire on the subject was carried out by the administration to five respondents in each category of healthcare professionals to ensure the reliability of data collection by the tool. Self-administration of validated questionnaires with written instructions was to doctors and nurses during out-patient department (OPD) consulting hours and also on inpatient wards (but explanation was carefully given to respondents to clarify areas that had difficulty in understanding). Pharmacists were consulted in the hospital pharmacies and some in the wards. To ensure a high response rate, questionnaires were administered, time was allowed for respondents to provide responses, and questionnaires were collected. Respondents were not allowed to take questionnaires away and return them at a later time. They were required to tick options on the questionnaire where applicable in the case of multiple-choice questions and write responses in cases where free space was allowed or applicable.

Data analysis

Data collected were entered into Statistical Package for the Social Sciences version 20, IBM, to obtain descriptive statistics such as frequency and percentages. Graphs were plotted using Sigma Plot version 11.0, Systat Software Inc. Bivariate correlation analysis was conducted with Pearson's (r) and chi-square (χ^2) correlation coefficient coupled with a two-tailed test of significance at confidence interval 95% to determine the level of association between test parameters.

Ethical Cconsiderations

The College of Health Science Ethical Committee granted ethical clearance before the commencement of the study (CHRPE/159/17). No form of incentive, remuneration, or relationship with tendencies of conflict of interest was tolerated. An in-depth exposition on the purpose of the study was given and informed consent independent of any external coercion or manipulation was obtained. The anonymity of the respondents was also ensured by randomly coding the semistructured questionnaire.

RESULTS AND DISCUSSION

Epidemiological data on TED burden, risk perception, and thromboprophylaxis practices in sub-Saharan countries like Ghana remain scanty. However, with TED being identified as a major contributor to preventable morbidity and mortality the world over (Aduful and Darko, 2007), it is important that there is local research to garner more insight.

Socio-demographics

Of 109 questionnaires administered, 105 (96.33%) were returned. The majority (46, 43.8%) of the respondents worked in a teaching hospital and were medical doctors (72, 68.6%) who were into GP, medicine, surgery, or obstetrics and gynecology and had an experience between 5 and 10 years (61, 58.1%) (Table 1).

Prevalence and risk perception

A greater proportion of respondents (90, 85.7%) were of the opinion that thromboembolism was a risk in their area of practice, with 49 (46.7%) rating the risk as medium and 8 (7.6%) rating the risk as high (Fig. 1A). The majority (49, 46.7%) indicated that thromboembolic conditions were reported often, with 55 (52.4%) indicating a more often observation at the inpatient ward than at the OPD (45, 42.8%). DVT (89, 24.3%) was the most commonly reported thromboembolic condition, closely followed by ISemic (64, 17.4%) (Fig. 1B), with pain (103, 31%) being the most common symptom reported (Fig. 1C).

There was no significant difference ($p > 0.05$, $\chi^2 = 3.66$, $r = -0.161$) in TED risk perception across the different specializations. In all specializations, a greater proportion of respondents were of the opinion that thromboembolism was a risk in their area of practice, i.e., gGP (33, 78.6%), medicine (21, 87.5%), surgery (31, 93.9%), and obstetrics and gynecology (5, 83.3%) (Fig. 2A).

There were significant differences ($p < 0.01$, $\chi^2 = 35.88$, $r = 0.411$**) in the rating of TED risk across different specializations. It was observed that the majority of respondents in GP 51.5%, medicine 47.6%, and obstetrics and gynecology 80.0%, rate the risk of TED as medium. However, in surgery, 54.8% of the respondents viewed TED as a high risk in their area of practice (Fig. 2B).

Table 1. Demographic characteristics of respondents in a survey for determining the TED burden in Kumasi, Ghana.

Demographics	Particulars	*n* (%)
Institution		
	Teaching Hospital	46 (43.8)
	Regional/District Hospital	22 (21.0)
	Poly Clinic	23 (21.9)
	Private Clinic	14 (13.3)
Professional background		
	Medical Doctor	72 (68.6)
	Nurse	20 (19.0)
	Pharmacist	13 (12.4)
Years of practice		
	<5 years	19 (18.1)
	5–10 years	61 (58.1)
	>10 years	25 (23.8)
Respondents specialization		
	GP	42 (37.2)
	Medicine	24 (21.2)
	Surgery	33 (29.2)
	Obs. & Gyne.	6 (5.3)
	Other specializations	8 (7.1)

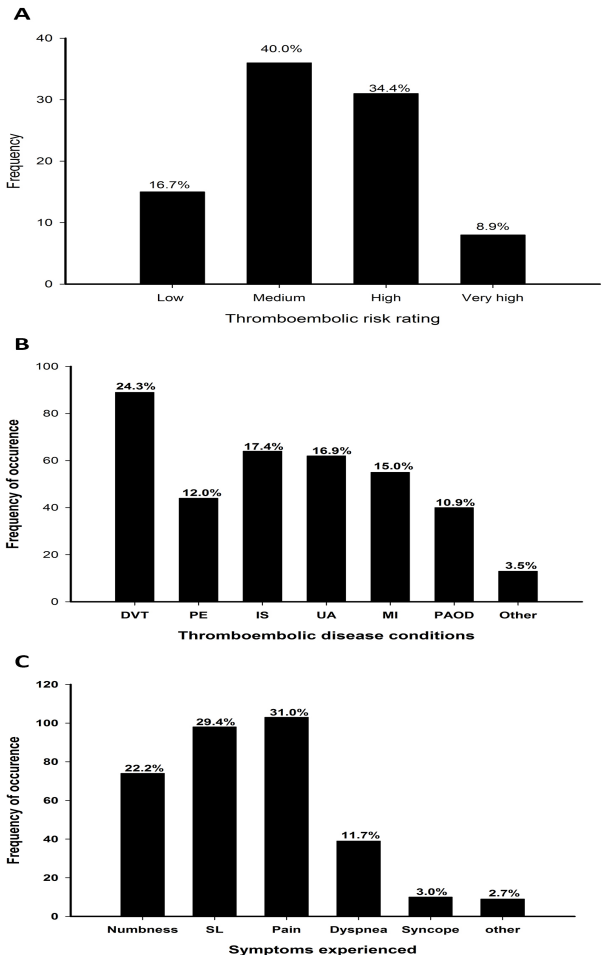

Figure 1. (A) Healthcare practitioners rating of thromboembolic risk in their areas of clinical practice. (B) Commonly reported thromboembolic conditions across different clinical specializations. (C) Commonly reported symptoms of thromboembolic conditions in hospitals according to health practitioners, in hospitals in Kumasi, Ghana (DVT = deep vein thrombosis; PE = pulmonary embolism; IS = ischemic stroke; UA = unstable angina; MI = myocardial infarction; PAOD = peripheral arterial occlusive disease; and SL = swollen limbs).

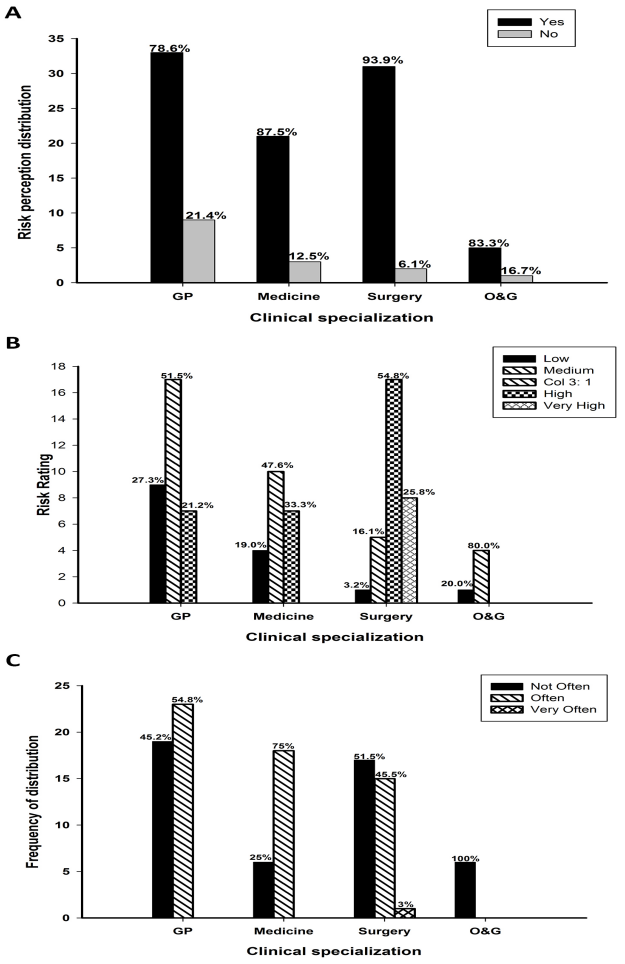

Figure 2. (A) TED risk perception across different clinical specializations. (B) TED risk rating across different clinical specializations. (C) Incidence of thromboembolic conditions across different clinical specializations in hospitals in Kumasi, Ghana (GP = general practice; O & G = obstetrics and gynecology).

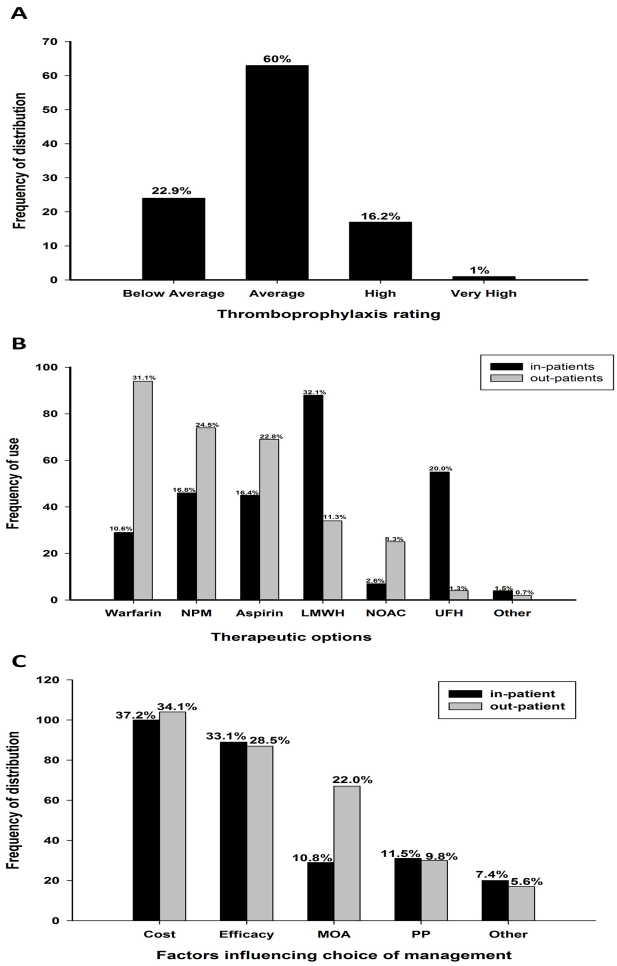

Figure 3. (A) Rating of practice of thromboprophylaxis in area of practice by health practitioners. (B) Therapeutic options employed in the management of TED in the OPD and outpatient setting. (C) Factors influencing the choice of management option of TED in the OPD and in-patient setting, in hospitals in Kumasi, Ghana (NPM = nonpharmacological management; LMWH = low-molecular-weight heparin; NOAC = new oral anticoagulants; UFH = unfractionated heparin; ROA = route of administration; and PP = personal preference).

There were differences in the incidence of thromboembolic conditions across different specializations. According to the majority of respondents in surgery (17, 51.5%) and obstetrics and gynecology (6, 100%), thromboembolic conditions were not often reported. However, 23 (54.8%) and 18 (75%) of respondents in GP and medicine, respectively, were of the opinion that thromboembolic conditions were often reported. These differences were however not significant ($p > 0.05$, $\chi^2 = 14.26$, $r = -0.132$) (Fig. 2C).

Findings of the study have identified TED as a significant health risk in Ghana. This is in line with other research publications that identified TED as a significant risk across different clinical specializations (Goldhaber, 2010). Several factors have been identified as major predisposition parameters. The main factors samong these are major orthopedic surgery, malignancies, congestive heart failure and respiratory failure, age, obesity, immobility, pregnancy, and use of oral contraceptives. These wide-reaching risk factors place most patients presenting at the various healthcare facilities (regardless of their health condition and clinical needs) at risk of TED, with its associated negative health implications. This could thus explain why the majority of respondents identified TED as a significant health risk and also why there was no significant difference in the report of TED across the different specializations.

Practice of prophylaxis and management outcomes

The majority (77, 73.3%), of the respondents were of the opinion that thromboprophylaxis was common in their area of practice. Also, despite thromboprophylaxis being common in the area of practice according to respondents, there were variations in the rating of the practice of thromboprophylaxis, with the majority of 63 (60%), respondents rating thromboprophylaxis as average in their areas of practice (Fig. 3A). Pharmacological management was the predominant form (105, 53.8%) of management and prophylaxis of TED, with 83 (79%) respondents indicating differences in the management of outpatients and inpatients.

In terms of therapeutic options employed in the management and or prophylaxis of TED, low-molecular-weight heparins (LMWH) (88, 32.1%) and warfarin (94, 31.1%) were the

predominantly used therapies in the inpatient (ward) and outpatient department (OPD) setting, respectively, with nonpharmacological management (NPM) (74, 24.5%) mainly employed in the OPD setting (Fig. 3B). Cost of therapeutic options also emerged as the most significant factor influencing the choice of management in both the OPD [100 (34.1%)] and inpatient [104 (37.2%)] settings. Also, the route of administration of therapy (ROA) significantly affected to a higher extent the choice of management option in the OPD setting [67 (22.0%)] compared to the inpatient setting [29 (10.8%)]. Also, according to 72 (42.9%) respondents, bleeding was the most common side effect reported, albeit not often reported, according to 96 (91.4%) respondents. Finally, according to the respondents, cost emerged as the greatest hindrance to patients going on and adhering to treatment (Fig. 3C). Thromboprophylaxis practice among healthcare practitioners and management outcomes is as shown in Table 2.

Prevalence of the practice of thromboprophylaxis across different specializations

Thromboprophylaxis was common across all specializations except in obstetrics and gynecology. The majority of respondents in GP (27, 64.3%), medicine (17, 70.8%), and surgery (31, 93.9%) were of the opinion that thromboprophylaxis was common. However, in obstetrics and gynecology, the majority of respondents (4, 66.7%) were of the opinion that thromboprophylaxis was not common. These differences were however not significant ($p > 0.05$, $\chi^2 = 13.909$, $r = -0.153$) (Fig. 4A).

Table 2. Thromboprophylaxis practice among healthcare practitioners and management outcomes in Kumasi, Ghana.

Thromboprophylaxis/management outcomes	Particular	n (%)
Prevalence of prophylaxis		
	Common	77 (73.3)
	Uncommon	28 (26.7)
Management		
	Pharmacological	105 (53.8)
	Non-pharmacological	90 (46.2)
Difference in management of OPD and in-patients		
	Yes	83 (79)
	No	22 (21)
Side effects of medications		
	Bleeding	72 (42.9)
	GI symptoms	64 (38.0)
	HIT	27 (16.1)
	None	5 (3)
Frequency of side effects		
	Often	4 (4)
	Not often	96 (96)
Hindrance to treatment		
	Cost	104 (65.0)
	Side effects	45 (28.1)
	Drugs not effective	6 (3.8)
	Other	5 (3.1)

GI = Gastrointestinal; HIT = Heparin-induced thrombocytopenia; OPD = Out-patient department.

Rating of the practice of thromboprophylaxis across different specializations

In assessing the rating of the practice of thromboprophylaxis across the different specializations, it was observed that majority of the respondents in GP (26, 61.9%) and medicine (19, 79.2%), a greater proportion of respondents, rated the practice of thromboprophylaxis as average. In surgery, however, even though the majority (16, 48.5%) of the respondents rated the practice of thromboprophylaxis as average, contrastingly, there was a significant proportion of respondents, (14, 42.4%) who rated the practice as high and some even very high, (1, 3.0%). In obstetrics and gynecology, however, a greater proportion of respondents, (4, 66.7%) rated the practice of thromboprophylaxis as below average, with the remaining respondents, (2, 33.3%) rating the practice as average. These differences were significant ($p < 0.01$, $\chi^2 = 42.711$, $r = 0.363$**) (Fig. 4B).

Respondents who rated TED as high or very high risk in their area of practice had a higher rate of thromboprophylaxis in their area of practice compared to those who rated TED as low risk. The majority of respondents who rated the risk of TED as low (9, 60.0%), medium (22, 61.1%), and high (19, 61.3%) rated

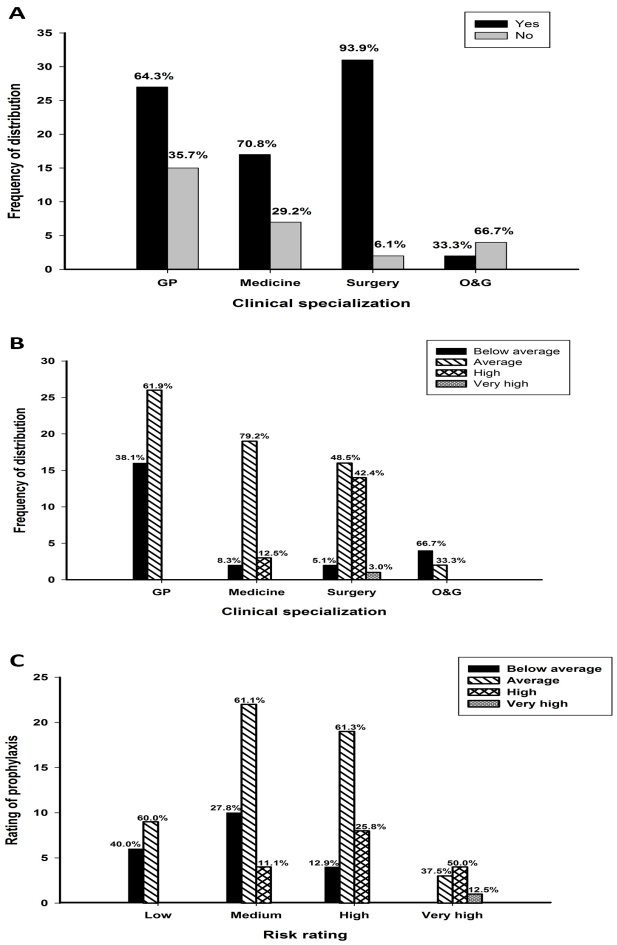

Figure 4. (A) Prevalence of the practice of thromboprophylaxis across different clinical specializations. (B) Rating of the practice of thromboprophylaxis across different clinical specializations. (C) Relationship between thromboembolic risk rating and rating of thromboprophylaxis, in hospitals in Kumasi, Ghana (GP = general practice; O & G = obstetrics and gynecology).

the practice of thromboprophylaxis as average. However, the majority of respondents (4, 50%) who rated the risk of TED as very high rated the practice of thromboprophylaxis as high. These differences were significant ($p < 0.01$, $\chi^2 = 25.92$, $r = 0.418$**) (Fig. 4C).

The study revealed that the risk of TED, however, may vary considerably depending on the risk factors and other cofactors present and is not the same in every area of practice or specialization. This was evidenced in the different ratings of the risk of TED as indicated by the respondents in the study. This research finding also agrees with literature and other published data on TED risk in different areas of clinical specialization (Gould *et al*., 2012). With patients presenting with different risk factors and also different clinical procedures such as type of surgery and length of hospital stay, patients subject to different exposure to risk of TED, it was not surprising that respondents from different clinical specialization background rated the risk of TED differently. For instance, from the study, surgery had the highest risk rating of TED as against GP. The difference in perception of risk could be due to the perceived differences in types of risk factors prevalent in each area of practice. Also, the lack of and nonuse of standardized risk assessment tools could lead to major risk factors being ignored resulting in reduced risk perception. The significantly higher risk perception in surgical practice could be as a result of the invasive nature of surgical procedures such as total hip and knee replacements which is associated with an exceedingly high risk of VTE. By nature of their practice, most surgeons are thus more aware of the thromboembolic risk and as such are more likely to take precautions, such as thromboprophylaxis than practitioners carrying out noninvasive procedures like in GP and medicine. This could also, therefore, explain the higher rating of the practice of thromboprophylaxis recorded in surgery as compared to the other specialties, with surgeons appearing to be more aware of the accompanying risks of their practice, as seen in this study. These findings agree with other previous publications which found a higher thromboembolic risk perception amongst surgeons than other health practitioners, with patients undergoing surgical procedures more likely to receive adequate prophylaxis than, for instance, medical patients (Cohen *et al*., 2008; Bâ *et al*., 2011).

Although the risk of TED was higher in surgical practice than the other specialties as shown in this study, TED was not often reported according to most respondents. This significant finding could be due to a better understanding of risk factors, improved risk identification, and also better thromboprophylaxis practice in surgical practice than the other specialties, as shown in this study. Also, the relatively higher numbers of thromboembolic cases recorded in GP and medicine as indicated by respondents could be significantly due to the relatively high incidence of cardiovascular cases, which are mostly seen in these clinics. This is because most of the patients who develop arterial thromboembolic conditions such as ISischemic often have other underlying cardiovascular diseases such as hyperlipidemia and atherosclerosis which makes them prone to TED (Verstraete, 1990). Also, the possible absence of credible epidemiologic data and institutional records on a number of thromboembolic cases recorded could also result in an over- or underestimation of the incidence of TED. This could negatively impact health policy and planning as the true impact of TED will not be known, knowledge of which could have positively influenced policy direction and resource allocation in curbing this health problem (Cushman, 2007).

Several research findings such as the ENDORSE and MEDENOX trials have sought to establish an increased risk of TED in hospitalized patients, with some research going as far as associating an increased risk of TED with an increased length of stay in the hospital (Greaves and Holubar, 2015). This increased risk of TED in hospitalized patients could often be as a result of reduced mobility (stasis), increased risk of infection, relatively much severe illness, and major procedures such as major surgeries of hospitalized patients compared to out-patients. This confirms the findings of this present study where most cases of TED were reported in the in-patient setting (Wards) compared to the out-patient setting.

DVT was the most commonly reported TED and accounts for about two-thirds of all venous thrombosis cases, with PE accounting for the remaining third (Raskob *et al*., 2014). DVT poses a significant health risk across different clinical specializations, with several research findings reporting increased cases of pregnancy-associated DVTs, increased risk of DVT in stroke patients presenting at medical departments, and also increased risk of DVT with orthopedic surgeries (Cohen *et al*., 2008; Cushman, 2007). This far-reaching incidence and impact of DVT across different clinical specializations could thus explain why DVT emerged as the most commonly reported TED. PE is often a complication of an untreated or poorly managed DVT. This could explain the low incidence of PE relative to DVT as a well-managed DVT will not result in a potentially fatal PE. Also, most PEs are often symptomless and misdiagnosed, with some PEs only diagnosed after autopsies. This could also explain the low incidence of PE as compared to DVTs, especially in Ghana where autopsies are not routinely done. DVT was followed by emicIS, unstable angina (UA), and myocardial infarction (MI) as the most commonly reported TED. IS, UA, and MI account for the majority of arterial thrombosis cases and related morbidity and mortality (Jackson, 2011). With an aging population and changing lifestyle, arterial TED risk factors such as high blood pressure, atherosclerosis, diabetes, and obesity are on the increase. This has led to an increase in cases of arterial TED such as IS, UA, and MI and could thus explain the high incidence of the report as shown in the study. With regard to common symptoms, the report of pain and swollen limbs (SL) as the most common symptoms was also not surprising as pain and SL or extremities are classical signs of DVT which according to respondents was the most commonly reported TED. Also, arterial TED such as UA and MI had pain as a common symptom. Pain associated with TED is often due to buildup of lactic acid and tissue damage as a result of reduced oxygen supply (Sutherland *et al*., 2000).

The coagulation cascade is amongst the most well-studied and well-understood systems in the human body, with several available proven and effective therapies for the management and prevention of TED. However, significant gaps still do exist in the prophylaxis and management of TED (Henke and Pannucci, 2010; Kearon *et al*., 2016). As shown in this study, despite thromboprophylaxis being common, there were wide variations with regard to the rating of the practice. Despite an improvement in the practice of thromboprophylaxis across board, several research findings have indicated the practice to be

woefully inadequate, with patients still at risk. Most patients even though receiving prophylaxis, the prophylaxis was found to be below the recommended standard prescribed by guidelines such as the American College of Clinical Pharmacy guidelines (Cohen *et al*., 2008). It was thus not surprising that most respondents rated the practice as either average or below average. Also, the difference in the rating of thromboprophylaxis across the different specializations could be linked to the differences in risk perception as evidenced in the study, with the highest rating of thromboprophylaxis seen in the highest thromboembolic risk rating category and vice versa. The differences in the practice of thromboprophylaxis could also be linked to the fear of risk of side effects such as bleeding as seen in, for instance, obstetrics and gynecology, where a low rate of thromboprophylaxis was observed. With pregnancy and delivery associated with a high risk of bleeding (postpartum hemorrhage), coupled with risk of bleeding as a side effect of anticoagulants like heparin and warfarin, clinicians may weigh the risk versus benefit of thromboprophylaxis and may opt for other means of prevention of TED such as nonpharmacological means as against thromboprophylaxis (Gibson and Powrie, 2009). This is of particular concern as pregnancy itself has been found to increases the risk of TED by up to fourfold. It is therefore important and critical to adopt and implement standardized risk assessment tools to pick up at-risk women and develop thromboprophylaxis protocols to protect at-risk groups (Heit *et al*., 2005).

Most research findings have identified pharmacological management as pivotal in the management of TED, with most guidelines recommending pharmacological agents which have been proven effective in the management and prophylaxis of TED and these have gone a long way to improve disease outcomes. This could thus explain the preference of pharmacological options in the management of TED according to the majority of respondents (Coleman and MacCallum, 2010).

Warfarin and aspirin were the most preferred therapy employed in the OPD setting and this could be closely linked to their route of administration, being oral compared to the other therapeutic options such as unfractionated heparin (UFH). Most patients may be prescribed warfarin and aspirin because they are oral and may be relatively easier to administer compared to UFH which is parenteral. However, the high number of respondents who selected LMWH even though it is also an injectable could be as a result of the subcutaneous administration of LMWH, the proven safety, minimal risk of bleeding, and also the predictable anticoagulant action, hence not requiring monitoring. Limited use of nonvitamin K antagonist new oral anticoagulants (NOAC) such as rivaroxaban, even though also oral, in the OPD setting, could be as a result of its high cost and the fact that it is a relatively new drug compared to the other therapeutic options and as such most clinicians are not so comfortable or conversant with its use. However, the relatively higher use of parenteral or injectable medication like LMWH and UFH in the in-patient setting could be as a result of their relatively cheaper cost and also the fact that their anticoagulant action is either predictable or can easily be monitored in the hospital setting. Also, most of these drugs are used in an emergency setting requiring immediate anticoagulant effect, something therapeutic agents like warfarin cannot achieve, requiring periods of titration to achieve optimal doses (Weitz and Linkins, 2007). Also, in assessing the factors affecting the choice of therapy in both the OPD and in-patient setting, cost featured prominently and this could explain the limited use of therapies such as rivaroxaban which is relatively more expensive compared to other oral therapies like warfarin and aspirin.

The issue of side effects even though not commonly reported cannot be ignored and significantly affect the choice of therapy in the management of TED. Side effects such as bleeding, gastrointestinal tract complications, and heparin-induced thrombocytopenia being the most commonly reported were not too surprising as such reports are known side effects commonly associated with the use of UFH, heparin, aspirin, and warfarin, which were the therapies commonly used from the study analysis (Gibson and Powrie 2009).

The cost of available therapeutic options for the management and prophylaxis of TED was the greatest hindrance preventing patients from going on and or staying on treatment. This is particularly important especially in low-income countries like Ghana where most patients fall into the nonaffordability bracket. This finding agrees with most publications that find available thromboembolic therapeutic options especially new oral anticoagulants like rivaroxaban particularly expensive compared to traditional anticoagulants like warfarin (Nutescu, 2013; Scaglione, 2013). These findings should thus inform policy, for instance, review of national health insurance scheme drug list to cover some of these newer medications to enhance access.

Use of herbal medicines in TED

With regard to patients reporting ever using herbal medicines in the management and or prophylaxis of TED to respondents, a greater proportion of respondents, (72, 68.6%) responded in the affirmative. However, according to 40 (55.6%) respondents, the use of herbal medicines in the management of thromboembolic conditions was about < 10% of the total number of patients they managed.

There were significant differences ($p < 0.05$, $\chi^2 = 7.456$, $r = 0.249$*) in the use of herbal medicines in the management of TED across the different specializations. It was observed that majority of the respondents across all specializations, i.e., GP (34, 81.0%), medicine (16, 66.7%), and surgery (20, 60.6%), reported their patients ever using herbal medicines to manage thromboembolic conditions except in obstetrics and gynecology, where the opposite was observed, with the majority of respondents 4 (66.7%) reporting their patients not using herbal medicines in the management of the thromboembolic condition (Fig. 5).

Although a significant proportion of patients reported ever using herbal medicines to manage thromboembolic conditions, however in relation to general hospital attendants in the orthodox setting, the proportion of patients reporting ever using herbal medicines were in the minority (less than 30%). This is however very insightful, as it reveals that at least three out of every 10 patients reporting to the orthodox setting might have used or even still using herbal medicines as a therapeutic option before reporting to the orthodox hospital. This is important to note as these patients may even be still on these herbal medicines before they are given orthodox medicines which could result in possible drug–drug interactions. Also, it shows that herbal medicines continue to remain an important therapeutic option employed by most

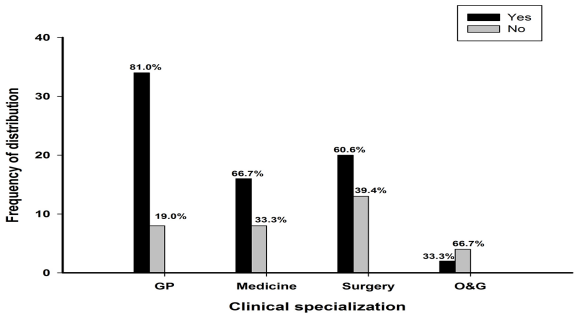

Figure 5. Patients' use of herbal medicines in the management of thromboembolic conditions across different clinical specializations in hospitals in Kumasi, Ghana (GP = general practice; O & G = obstetrics and gynecology).

Ghanaians and as such efforts need to be made to improve their efficacy and safety and possibly integrate their use in mainstream orthodox practice. These findings agree with previous research findings which revealed that a significant proportion of people still use herbal medicines in the management of many disease ailments including thromboembolic and cardiovascular diseases and warned of possible drug interactions (Mashour *et al*., 1998).

However, notable differences were seen in the use of herbal medicines across the different specializations, with the least observed in obstetrics and gynecology and highest in GP. These differences in the use of herbal medicines across the different specialties could be linked to the different types of thromboembolic conditions and risks presenting at the different specializations. Most cases in GP and medicine are seen on OPD bases and such patients may have access to herbal medicines to use in management. Also, most GP and medicine cases are chronic or have long-term risks requiring most often long-term prophylaxis. These patients are often seen as OPD cases and are most likely to have access to the use of herbal medicines, unlike surgical patients who often have short-term risks and are often seen as in-patients. The limited use of herbal medicines by patients in the obstetrics and gynecology (O & G) department could be as a result of the cautions associated with pregnancy, with most patients advised not to take any medications without the prior consent of their doctor. The advice given to patients about the possible safety concerns of certain medications including herbal medicines could be a strong deterrent for many patients and could account for the limited use of herbal medicines in O & G.

A study by Frawley *et al*. (2015) reported that more women were most likely to take herbal medicines for diseases, such as varicose veins, with most of these herbal medicines also being self-prescribed. Furthermore, herbal medicines use in pregnancy was more common in the rural setting than in the urban setting. This agrees with the findings of this study which reported the use of herbal medicines by pregnant women in the management of TED. The relatively smaller percentage of patients reporting ever using herbal medicines in pregnancy could be due to the urban setting of this study. There could be a probability of higher use of herbal medicines in pregnancy if this study was carried out in the rural setting.

CONCLUSION

Findings from the study have identified TED as a significant health risk in Ghana as healthcare professionals are of the opinion that thromboembolism was a risk across all the different clinical specializations of practice. Thromboprophylaxis is however practiced averagely in all areas of practice because of the high cost of therapy. Therefore, although therapies for management and prophylaxis of TED are available and effective, it is still a burden and perceived as a risk in clinical practice and healthcare delivery in Ghana.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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