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Prevalence of bleeding symptoms among young adults in Saudi Arabia, a national survey

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Abstract

Prevalence of bleeding disorders vary due to several factors including geographical location. Mild bleeding disorders can lead to iron deficiency, morbidity, and in severe cases mortality. Quantification of haemorrhagic symptoms is a key component in management of bleeding disorders and a challenging task for clinicians.

An abridged version of MCMDM-1vWD questionnaire with validated Arabic translation was used to quantify bleeding disorders in adult students ($n = 1138$) in 4 different regions of Kingdom of Saudi Arabia. Statistical analysis was performed to indicate gender disparity and prevalence.

74.5% of respondents answered at least 1 question with affirmation, with 32.3% affected in Riyadh showing the highest prevalence and 14.03% affected in Dammam showing the least prevalence (P-value $< .001$). Gender-wise, higher prevalence of bleeding disorders in females 54.9% than in males 45.1% was observed (P-value .01). Epistaxis prevalence was significantly higher in males 30.7% vs 23.2% in females (P-value .0004), while cutaneous symptoms were reported significantly more by female participants 29.7% vs 12.3% in males (P-value $< .001$). Menorrhagia was reported by 28% of females, with heavy bleeding experienced by 57.6% female participants for <7 days while in 42.4% of females for >7 days.

The current study signifies the ethnic distribution and gender disparity of mild bleeding disorders, and highlights the need for national surveillance system in order to improve management of patients with bleeding disorders.

Abbreviations: BAT = bleeding assessment tools, KSA = Kingdom of Saudi Arabia, MBD = mild bleeding disorders, MCMDM-1vWD = molecular and clinical markers for the diagnosis and management of type-1 von Willebrand disease, vWD = von Willebrand disease.

Keywords: bleeding, coagulation, inherited

1. Introduction

Bleeding symptoms indicate otherwise hidden haemostatic disorders and are relatively common amongst the general population. Bleeding symptoms such as epistaxis (25%), menorrhagia (47%), easy bruising (18%), and prolonged bleeding due to dental extraction (18%) have been reported in otherwise healthy adults.[1] However, severe bleeding symptoms as a sign of bleeding diathesis usually develop in the form of a

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cluster in patients with bleeding disorders.[2] Using different methods of estimation, the prevalence studies report varying rates of bleeding disorders across the globe.[3–5] According to estimates by Sadler,[6] 25% of males and 46% of females suffer from at least 1 bleeding symptom/underlying bleeding disorder. Besides severe bleeding disorders, correct diagnosis is also necessary to decide on preventive measures for mild bleeding disorders (MBD) including, platelet function disorders, mild von Willebrand disease (vWD), and mild clotting factor deficiencies. Although MBD do not cause higher mortality yet can pose as a potential reason for intervention of hemostatic agents and blood products during and after surgical procedures to control bleeding and mild chronic bleeding. Diagnostic criteria are more conflicting for MBDs compared to severe bleeding disorders.[7]

Various tools have been standardized and validated to identify patients with bleeding symptoms and an indication of a bleeding disorder.[8,9] Bleeding questionnaires with scores known as bleeding assessment tools (BAT) have been widely used for this very purpose since the introduction of the classical concept of BAT in 1982.[8] In the updated Vicenza-based BAT, the bleeding score ranges from zero (absence of any bleeding symptom) to 3 (bleeding symptoms in need of intervention), while the total score is a sum-of-scores of all bleeding symptoms.[10] Later on, to enhance the sensitivity and specificity of bleeding scoring system, Tosetto et al[11] evaluated the bleeding severity in a large panel of type-1 vWD families enrolled in a European study called the "molecular and clinical markers for the diagnosis and management of type-1 von Willebrand disease" (MCMDM-1vWD). Bowman et al[7] further condensed the MCMDM-1vWD and cross validated it for clinical utility, reproducibility and validity.

Hematologists[12] and anaesthesiologists[13] have provided a list of guidelines for the assessment of bleeding risk prior to invasive procedures, through bleeding histories along with physical examination. The benefits of laboratory testing, and questionnaires include better management during surgical interventions and emergency department visits.

The prevalence of bleeding disorders doesn't follow the same trend over all ethnic groups. Moreover, in western developed countries, hereditary bleeding disorders have been well-documented during the past 70 years,[14–17] yet the studies reporting the prevalence of bleeding disorders in developing countries remain scant.[18] Difference in assessment tools is another hurdle in cumulative risk identification and prevalence assessment. Prevalence reports from the Middle east, specially Saudi Arabia, are institution based relying upon laboratory testing[19] or previous medical records,[20] however, MCMDM-1vWD is rarely used for screening despite its clinical utility and validity.

Owing to high consanguinity, the Arab population is more prone to bleeding disorders than their western counterpart.[21–23] A population-based bleeding symptom survey could help identify patients with critical bleeding disorders and hence provide better management during hospital visits, as well as evaluation of population prone to iron deficiency due to bleeding issues.

2. Methods

The multicentre IRB approval was obtained from King Faisal Specialist Hospital and Research Centre and King Saud University in Riyadh; Taibah University in Medina; Umm alQura University in Makkah, and Imam Abdulrahman Bin Faisal University in Dammam.

An epidemiological survey was carried out on a randomly selected young Saudi adults of both genders, using a semi-structured validated and condensed MCMDM-1vWD bleeding assessment questionnaire. This questionnaire was selected owing to its capacity to generate quantifiable data from the entire study group.[9] The process of translation and validation into Arabic and adaptation of MCMDM-1vWD for implementation had been published.[24] The questions and sub-questions are detailed in (Appendix 1, Supplemental Digital Content, http://links.lww.com/MD/G459). There are 10 questions examining different bleeding symptoms, including commonly reported: epistaxis, cutaneous and oral symptoms, and menorrhagia.

For the survey, an interview of a "nationally representative" group of 1138 volunteering young adults from 5 different universities in 4 different regions of the Kingdom of Saudi Arabia (KSA) between May 2016 and 2018 was conducted onsite by trained Arabic speaking interviewers. Advertisement on each of the participating sites encouraged participation on first come first serve basis. Only those participants giving a positive response to any primary question were further sampled for lab testing. To reduce the subjectivity, we showed participants an educational pamphlet illustrating pictorial format, for example, to clear the difference between Ecchymosis, Hematoma, and Petechiae.

Based on the previous study where the prevalence of bleeding disorders in less than 14-years-old participants was studied in central region of KSA, and data from 3881 school students – we expanded the study in young university students to include other regions and major cities of KSA, that is, Makkah, Madinah, Dammam along with Riyadh. According to literature estimates, we calculated to include 200 patients minimum in each region, but to improve the accuracy and confidence interval for the extended laboratory study which will be published later, we included $n = 1138$ students.

The study was designed and carried out as a large national study generating several sub-studies with different lab tests conducted as part of this survey.

2.1. Statistical analysis

Descriptive statistics were computed as baseline: frequencies and percentages for categorical variables; and mean, standard deviation, minimum and maximum values for continuous variables. Precision-of-point estimates were estimated using 95% confidence intervals. Bleeding questionnaire variables were compared based on gender difference. Chi-square analysis was used to identify the significant change in percentage values when comparing bleeding variables to gender and city. Radar graph and bar graphs were used to show the prevalence of bleeding variables. We used the software STATA v.13.0 (Stata Corp., College Station, TX) in our analysis. A statistical significance threshold of $P < .05$ was adopted. No attempt at imputation was made for missing data.

3. Results

Number of medical students surveyed for bleeding symptoms was 1138, out of which 600 (52%) were females and 538 (48%) were males. There was a significant difference (P-value $< .001$) in gender balance between different institutes, with a female preponderance in Riyadh 190 (31.7%), Makkah (25%), and Dammam 111 (18.5%); while lower female to male ratio was observed in Medina: 149 (24.6%). Mean age for female students

was 19.7 ± 1.9 (range: 15.6–28.8 years), and male was 19.9 ± 2.4 (range: 15.9–30 years). We analysed our data based on gender disparity across variables that showing significant difference of proportions (Table 1). We used results from all sections to infer the bleeding prevalence among young Saudi adults.

Epistaxis was present in 138 (23.2%) females and 164 (30.7%) male participants (*P*-value < .004). Bleeding was observed in both nostrils by 55 (41.4%) females and 89 (55.6%) male participants (*P*-value < .013). Cessation was spontaneous in 35 (26.1%) females and 58 (36.5%) males; after short compression in 93 (69.4%) females and 100 (62.9%) males, and by medical intervention in 6 (4.5%) females and 1 (0.6%) male participants (*P*-value .024). Maximum age of severity was < 14 years among 73 (58.5%) females and 67 (44.7%) male participants, with a decrease in percentage of female 52 (41.6%) vs male 83 (55.3%) for age range of 14 to 45 years (*P*-value < .023).

Cutaneous symptoms were present in 178 (29.7%) females and 66 (12.3%) males (*P*-value < .001). Most common type was Ecchymosis in 139 (85.8%) females and 31 (79.7%) males (*P*-value .042). Medical attention was required in 22 (12.7%) females and 13 (25.5%) males (*P*-value .029). **Bleeding from minor wounds** was reported higher in 99 (16.5%) females and 68 (12.6%) male participants (*P*-value 0.06); with 1 to 5 times in 29 (37.2%) females and 26 (50%) of males, 6 to 12 times in 26 (33.3%) females and 12 (23.1%) males, while >12 times in 17 (21.8%) females and 4 (7.7%) of males (*P*-value 0.023). **Cutaneous bleeds** were mostly in exposed body area in 66 (91.7%) females and in 43 (93.5%) male participants (*P*-value .014). **Oral Bleeding** was present in 224 (37.3%) females and 238 (44.2%) male participants (*P*-value .018). Source of bleeding was gums in 59 (39.1%) females and 73 (61.3%) male participants (*P*-value < .001), and lip or tongue bite in 35 (28.7%) females and 10 (13.9%) males (*P*-value .018). Medical attention was sought in 28 (12.7%) females and 14 (6.5%) of the male participants (*P*-value .027). **GI bleeding** was present in 44 (7.3%) females and 26 (4.8%) male participants (*P*-value .08). Out of those reporting GI Bleed: blood in vomit was present in 12 (37.8%) female and 10 (43.5%) males, Melena in 9 (23.1%) female and 7 (26.9%) males, and blood in stool in 25 (61%) female and 6 (25%) male participants (*P*-value .005).

Bleeding due to surgery was experienced by 107 (17.8%) females and 90 (16.7%) male participants (*P*-value .623). Most significant cause was dental procedures in 35 (29.2%) females and 9 (10%) of male participants (*P*-value < .001), followed by abdominal surgery in 17 (15.9%) females and 13 (14.4%) male participants (*P*-value .770), and other surgical procedures causing bleeding in 9 (20%) females and 11 (55%) males (*P*-value .005). **Intramuscular or joint bleeding** was reported by only 12 (2%) females and 10 (1.9%) of male participants (*P*-value .84). Average rate of bleeding per year was 1 to 2 times in 5 (50%) of male participants and more than 2 times in 3 (25%) female participants. **Menorrhagia** was reported by 168 (28%) females, with heavy bleeding experienced by 95 (57.6%) female participants for <7 days while in 70 (42.4%) females for >7 days. Average duration of menstruation of less and more than 5 days was equally distributed (50%) across female participants. Consultation was sought by 11 (6.5%), while 19 (11.3%) underwent procedure, D&C in 1 (0.6%), iron supplements were used by 4 (2.4%) of participants.

Finally, we present overall prevalence of first 6 causes of bleeding in the form of a radar graph in Figure 1. It is observed that for Epistaxis, Cutaneous symptoms and oral bleed the male

Table 1

Prevalence of causes of bleeding in young adult Saudi Population.

City	Females n (%)	Males n (%)	*P*-value
Dammam	111 (18.5)	99 (18.4)	
Riyadh	190 (31.7)	109 (20.3)	
Makkah	150 (25)	95 (17.7)	
Medina	149 (24.8)	235 (43.7)	
Total	600 (100)	(100)	
1. Epistaxis	Female	Male	*P*-value
Yes	138 (23.2)	164 (30.7)	.004
1.1 Both nostrils	Female	Male	*P*-value
Yes	55 (41.1)	89 (55.6)	.013
1.2 Cessation	Female	Male	*P*-value
Spontaneous	35 (26.1)	58 (36.5)	.024
After short compression	93 (69.4)	100 (62.9)	
By medical intervention	6 (4.5)	1 (0.6)	
1.3 Max. age of severity	Female	Male	
14 to 45	52 (41.6)	83 (55.3)	.023
<14 years	73 (58.4)	67 (44.7)	
2. Cutaneous symptoms	Female	Male	*P*-value
Yes	178 (29.7)	66 (12.3)	<.001
2.1 Type	Female	Male	*P*-value
Ecchymosis	139 (85.8)	31 (79.5)	.042
Hematoma	14 (8.6)	8 (20.5)	
Petechiae	9 (5.6)	0	
2.2 Medical attention	Female	Male	*P*-value
Yes	22 (12.7)	13 (25.5)	.029
3. Bleeding minor wounds	Female	Male	*P*-value
Yes	99 (16.5)	68 (12.6)	.06
3.1 Number of episodes	Female	Male	*P*-value
<1	6 (7.7)	10 (19.2)	.023
1 to 5 times	29 (37.2)	26 (50)	
6 to 12 times	26 (33.3)	12 (23.1)	
>12 times	17 (21.8)	4 (7.7)	
3.2 Location of cut. Bleed	Female	Male	*P*-value
Exposed body area	66 (91.7)	43 (93.5)	.014
Un-exposed	6 (8.3)	0	
Both	0	3 (6.5)	
4. Oral bleeding	Female	Male	
Yes	224 (37.3)	238 (44.2)	.018
4.1 Gum source	Female	Male	
Yes	59 (39.1)	73 (61.3)	<.001
4.2 Lip or tongue bite	Female	Male	
Yes	35 (28.7)	10 (13.9)	.018
4.3 Medical attention	Female	Male	
Yes	28 (12.7)	14 (6.5)	.027
5. GI bleed	Female	Male	
Yes	44 (7.3)	26 (4.8)	.08
5.1 Blood in vomit	Female	Male	
Yes	14 (37.8)	10 (43.5)	.069
5.2 Melena	Female	Male	
Yes	9 (23.1)	7 (26.9)	.72
5.3 Blood in stool	Female	Male	
Yes	25 (61.0)	6 (25.0)	.005
6. Surgery	Female	Male	
Yes	107 (17.8)	90 (16.7)	.623
6.1 Major abdominal	Female	Male	
Yes	17 (15.9)	13 (14.4)	.779
6.1 Major chest	Female	Male	
Yes	1 (0.9)	1 (1.1)	.362
6.3 Dental	Female	Male	
Yes	31 (29.2)	9 (10)	.001
Others	Female	Male	
Yes	9 (20)	11 (55)	.005

(*continued*)

Table 1
(continued).

City	Females n (%)	Males n (%)	*P*-value
7. Muscle/hemarthrosis	Female	Male	
Yes	12 (2)	10 (1.9)	.86
7.1 Average rate per year	Female	Male	
1 to 2 times	0	5 (50)	.005
>2 times	3 (25)	0	
8. Menorrhagia	Female	Male	
Not Sure	23 (3.8)	N/A	
Trivial	3 (0.5)	N/A	
Yes	168 (28)	N/A	
8.1 Average periods in days	Female	Male	
<5 days	81 (50)	N/A	-
>5 days	81 (50)	N/A	
8.2 Heavy bleeding in days	Female	Male	
< 7	349 (61.9)	N/A	-
>7	215 (38.1)	N/A	
8.3 Only consultation	Female	Male	
Yes	11 (6.5)	N/A	
8.4 Procedure done	Female	Male	
Yes	19 (11.3)	N/A	
8.3 D&C	Female	Male	
Yes	1 (0.6)	N/A	
8.3 Use of iron supplements	Female	Male	
Yes	4 (2.4)	N/A	

to female prevalence percentage was highly skewed. In other cases, the difference of percentage was not that significant. In Table 2, we presented regional distribution of bleeding symptoms based on number of positive responses. With at least 1 positive response, the overall prevalence was 848 (74.5%), with Riyadh 274 (32.3%) showing highest prevalence and Dammam showing the least prevalence 119 (14.03%) with a significant variation in percentage among cities (*P*-value < .001). Gender-wise, we observed a higher prevalence in female 466 (54.9%) than males 382 (45.1%) which turned out to be significant (*P*-value .01), see Table 3. Based on 3 or more positive answer criteria, the prevalence was 199 (17.5%), with Riyadh 92 (46.2%) showing the highest and Dammam with 13 (6.5%) showing least prevalence (*P*-value < .001). Gender-wise results again showed higher prevalence in females 134 (67.3%) than males 65 (32.7%) for 3 or more answers.

We ran a regression to find an association between surgery related bleeding and epistaxis, cutaneous, oral symptoms, and we didn't find any significance in predicting bleeding during surgery. Menorrhagia had a significant inverse relation between surgery and menorrhagia (*P*-value < .001), Table 4. Figure 2 shows the percent of number of times participants responded positively. The distribution shows decrease in percentage with an increase in reported symptoms.

4. Discussion

There are several causes of bleeding in young adults and elderly, including immune thrombocytopenia, which is a common cause of hemorrhagic syndrome.[2,5] Symptoms including epistaxis, gingivorrhagia, GI bleeding, and menorrhagia can be seen in acquired as well as inherited bleeding disorders. Qualitative and quantitative perturbance in platelets and plasma proteins can lead to inherited bleeding disorders. Accurate evaluation of bleeding symptoms is a key element in clinical management of bleeding disorders. However, quantification of bleeding disorders based upon symptom is a cumbersome and challenging task for which several different questionnaires have been formulated to standardize the process. In the current study, we used condensed MCMDM-1vWD bleeding questionnaire which provides the ability to efficiently score the bleeding symptoms leading to

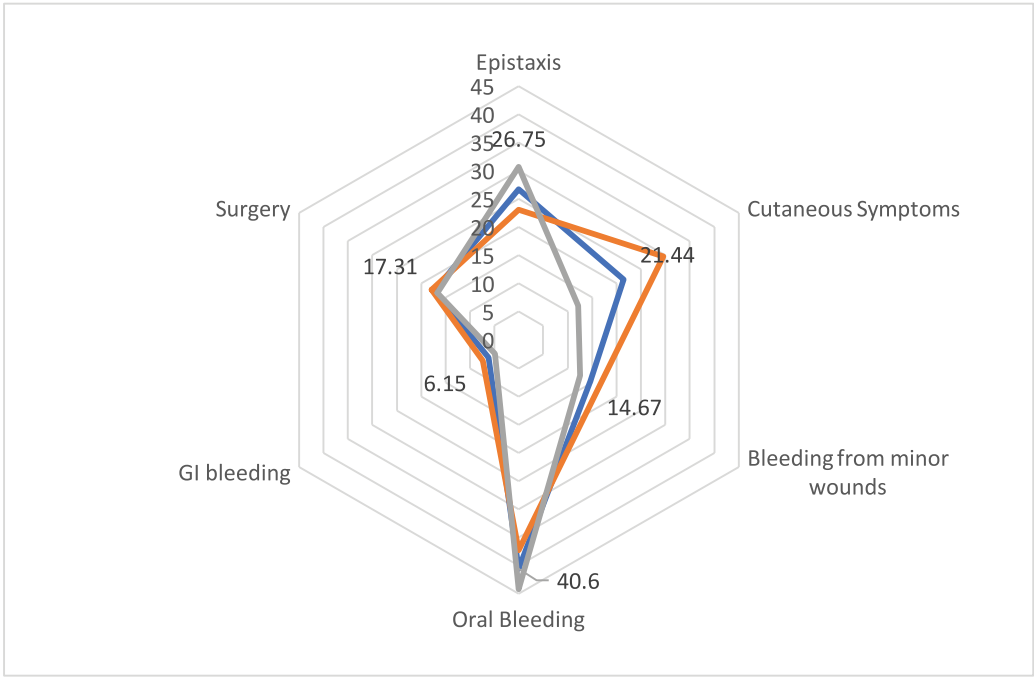

Figure 1. Radar graph for Bleeding causes to show prevalence in total population in "blue"; male population "gray" and female population in "orange".

Table 2

City-wise Bleeding symptoms distribution as per number of positive responses.

Bleeding	Dammam	Riyadh	Mecca	Medina	Total	*P*-value
No bleeding	91 (31.4)	25 (8.6)	76 (26.2)	98 (33.8)	290 (25.5)	
At least one	119 (14.03)	274 (32.3)	169 (19.9)	286 (33.7)	848 (74.5)	<.001
0 to 2 positive	197 (21)	207 (22)	211 (22.5)	324 (34.5)	939 (82.5)	
3 or more	13 (6.5)	92 (46.2)	34 (17.1)	60 (30.1)	199 (17.5)	<.001

identification of bleeding disorders. The MCMDM-1vWD offers diagnostic accuracy and reproducibility amongst observers and summarizes clinical information to prioritize further laboratory testing. Quantification of haemorrhagic symptoms was performed by Arabic translated questionnaire, this method provides potential advantages as compared to binary classification system and assess variability in bleeding severity facilitating improved treatment strategies.[7]

In lieu of epidemiological surveys, several intuitional-based studies assessed prevalence of inherited bleeding disorders on smaller scale in Saudi population, however, the focus and scope of these studies have been vWD, haemophilia A, haemophilia B, and platelet disorders.[23–25] El-Bostany et al[20] evaluated prevalence of vWD, haemophilia A, haemophilia B, and platelet disorders in 43 children, while Ahmed et al[26] reported 15 cases of haemophilia, 1 case of VII deficiency, 1 case of X deficiency and 12 cased of Glanzmann thrombasthenia. Al-Sharif et al[27] reported 17 cases with factor XIII deficiency in Riyadh region. In an 8-year retrospective analysis in 168 patients in Riyadh, Al-Fawaz et al[18] reported 57 cases of haemophilia, 25 cases of vWD, 18 cases of Glanzmann thrombasthenia, 18 cases of Bernard-Soulier disease, and 16 cases of clotting factor deficiencies. Nevertheless, there is a dearth of studies reporting MBD in Saudi population. The current study used MCMDM-1vWD to evaluate geographical distribution and gender disparity of MBDs in 4 different regions of KSA: Dammam, Riyadh, Makkah, and Medina.

In the current study, overall prevalence was 74.5% in young Saudi adults, with Riyadh showing the highest prevalence (32.3%), and Dammam showing the lowest prevalence (14.03%), demonstrating a significant variation in percentage among cities (*P*-value < .001). A previous study published by the same authors reported bleeding disorder prevalence to be 47.6%, but the study cohort contained younger population pool and from central region alone.[21] The gender disparity in our study was significant in epistaxis and cutaneous symptoms where male to female prevalence was skewed. Epistaxis was significantly higher in males 30.7% vs 23.2% in female participants of our cohort (*P*-value .0004). A similar trend of gender disparity in epistaxis was previously reported in bleeding symptoms survey in Riyadh, where 49.7% males and 35.8% females were affected.[21] Hussain et al,[28] Khan et al,[29] and Corbridge et al.[30] reported that males were affected by epistaxis twice more than the females in Asian and western population depicting biological reasons behind this trend rather than ethnic differences. The skewed prevalence of these inherited disorders in men due to X chromosome effect, and association of these bleeding disorders with epistaxis explains the high prevalence of epistaxis in the current study.

Contrarily, cutaneous symptoms occurred more commonly in females 29.7% than males 12.3%, and same trend we observed previously in Riyadh with 44.5% prevalence in females vs 17.6% in males.[21] One of the significant reasons for cutaneous bleeding was minor bruising, that is, Ecchymosis. Several studies covering easy/minor bruising reported these symptoms as being more in women than in men.[2,31,32] One major reason of this disparity can be more thickness of skin in men as compared to women[33] resulting in more secure minor vessels. Menorrhagia was reported by 28% of females while consultation was sought by only 6.5% of them. In a study from Turkey, 22% healthy females reported menorrhagia depicting effect of geographical and ethnic differential prevalence,[34] while in an Australian study, bleeding disorders were prevalent in 10.4% girls suffering from menorrhagia.[35] Detailed evaluation of menorrhagia is subject of another study, and will be reported in detail separately. In other symptoms, the difference of frequency was not significant.

Abu-Douleh et al[19] reported 36.5% bleeding prevalence in students by considering 2 positive responses as a sign of bleeding disorder. The high prevalence is important, as Arab populations have a higher prevalence of bleeding disorders than Western population, primarily due to the increased consanguinity ratio in Arab communities.[23] The current study provides prevalence information with respect to geographical distribution and genetic disparity of various bleeding disorders signifying the requirement for surveillance-system to identify and register individuals with bleeding symptom. Moreover, gender disparity clearly highlights the need for genetic mapping to identify the families and individuals at risk.

Table 3

Gender-wise bleeding symptoms prevalence as per number of positive responses.

Bleeding	Female	Male	*P*-value
No bleeding	134 (46.2)	156 (53.8)	
At least 1 positive	466 (54.9)	382 (45.1)	.01
0 to 2 positive	466 (49.6)	473 (50.4)	
3 or more positive	134 (67.3)	65 (32.7)	<.001

Table 4

Chi-2 analysis between surgery and epistaxis, cutaneous, oral and menorrhagia related bleeding.

	Surgery		
Variables	No	Yes	*P*-value
Epistaxis	247/302	55/302	.62
Cutaneous	204/244	40/244	.67
Oral bleed	370/462	92/462	.054
Menorrhagia*	121/168	47/168	<.001

* Done only among female participants.

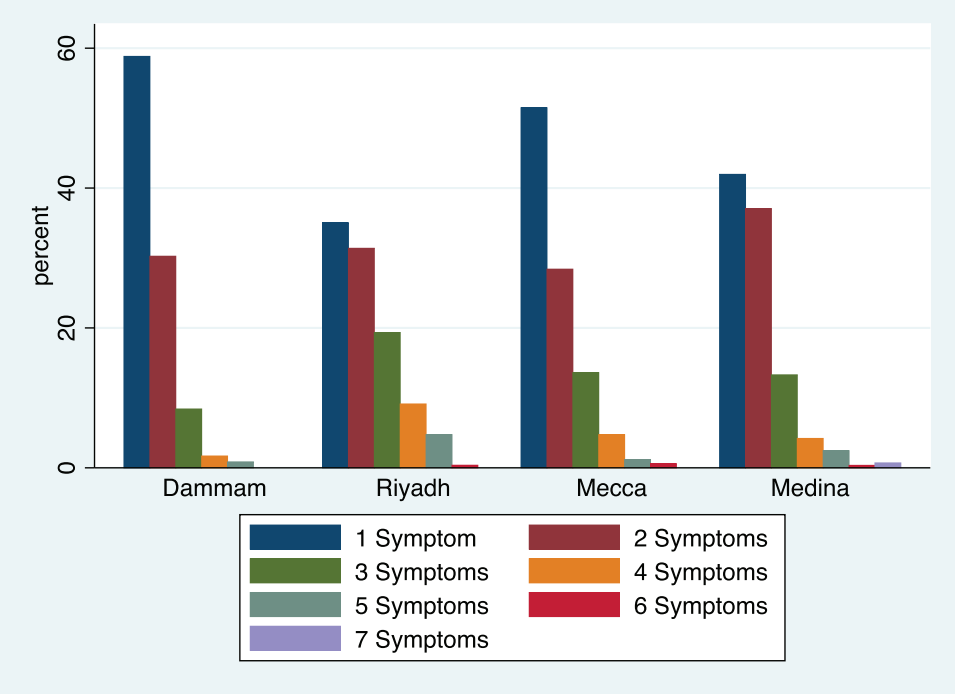

Figure 2. Percentage of participants reporting from 1 to 7 symptoms (1 means any one of the questions was answered in positive) in each city.

4.1. Limitations

Some of the limitations of the current study include lack of laboratory testing and its correlation with results obtained from the questionnaire. This will, however, be elaborated in later studies.

5. Conclusion

Identification of bleeding disorders can affect clinical management with improved patient outcomes. The current study is the largest epidemiological survey-based study which reports the prevalence of bleeding symptoms in young Saudi adults from 4 different regions of Kingdome of Saudi Arabia. Overall prevalence of bleeding disorders was 74.5% and gender-wise significantly higher prevalence in females 77.7% vs 71% males. High prevalence rates demand national surveillance system and genetics mapping in order to identify families at a higher risk. Prevalence survey at national level can lead to improved management of facilities at local hospitals pertaining to bleeding disorders.

Author contributions

KS and TO designed and developed the study. MZ and FZ were responsible for contents and authenticity. NA, AA, OK, KS, FA, AA, RS oversaw data collection, data entry, final review of data and analysis, were responsible for direction of the study team, and facilitation of the project plan.

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