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Relationship between Parenting Styles and Temper Tantrums of Bahraini Children Aged 24-48 Months Old at Primary Care, Kingdom of Bahrain

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Editorial

Original Contribution

Editorial

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This is sixth issue this years with papers touching on important issues for primary care in the Region.

Alhudaithi et al., did a cross-sectional population study looking at the Knowledge and Awareness of the Public toward Pediatric Eye Health and Diseases in Aseer region, Saudi Arabia: A Cross-Sectional Population Study. They stressed that pediatric ophthalmic conditions are a common and a serious public health problem, as they can not only impact the child's ability to learn, have a normal social life, and get a better quality of life, but they can also lead to complete blindness or visual impairment. Early intervention is necessary for childhood eye diseases since they can result in ongoing issues. The underlying causes of blindness in children differ significantly from region to region, depending on some factors, including socioeconomic development and access to primary healthcare services and facilities. However, it is estimated that there are over 19 million people globally with visual impairments and that there are roughly 1.4 million cases of blindness. As a result, the purpose of this study is to assess the parents' and caregivers' awareness in Aseer, Saudi Arabia, about various common pediatric ophthalmic diseases, including strabismus, amblyopia, refractive errors, and congenital glaucoma. By identifying the gap in knowledge and awareness, this could help create targeted educational and awareness programs geared toward the parents and the public of Aseer, Saudi Arabia, which could help prevent or reduce the prevalence of pediatric ophthalmic conditions, and boost the children's eye health

Selaibeekh, et al., did a cross-sectional, looking at Relationship between Parenting Styles and Temper Tantrums of Bahraini Children Aged 24-48 Months Old at Primary Care, Kingdom of Bahrain. The authors used a descriptive study design was employed, and a non-probability convenience sampling method was utilized to recruit a sample of 400 participants, that included 8 health centres located in Bahrain (Muharraq, BBK Hidd, Jidhafs, Sitra, Hamad Kanoo, Yousef Abdulrahman Engineer, Mohammed Jassim Kanoo, and Sh. Jaber Al Ahmed Al Sabah HCs,for a duration of 3 months(May 2022 to July 2022) The analysis technique employed was the chi-square test, a statistical method that is used to examine the association between two categorical variables. The authors stressed that Temper tantrums are episodic, unmodulated displays of intense emotional distress, often characterized by outbursts of anger, and may involve aggressive or destructive behaviour. These episodes can be effectively managed through the application of evidence-based parenting strategies that are tailored to a child's individual needs and developmental stage. The findings of this study demonstrated that more than half of the participating children exhibited temper tantrums that lasted more than 30 mins and showed that approximately less than one-third (31%) of the children experienced weekly or daily tantrums: however, half of the parents reported that moderate tantrums were exhibited by their youngsters. The most frequently reported tantrum behaviour was "crying", followed by "screaming" or "shouting". A child's request for an item or activity was the most frequent cause, and most tantrums occurred when their parents denied this request. Children threw temper tantrums most frequently in their homes or cars. Parents' most common strategy for stopping a child's tantrums was speaking soothingly, with spanking being the least common. The results indicated that permissive parenting styles were associated with a higher frequency of temper tantrums than authoritative parenting styles. The authors concluded that the results highlight significant aspects of tantrums, such as the duration, as children managed to maintain a tantrum episode for more than seven minutes on average. Tantrum behaviours, reasons, locations, context, and parents' strategies to control tantrums were emphasized as significant for developing proper interventions. The findings highlight the importance of parental styles in the development of children and the need for further investigation in this area.

Helvaci.., et al., looked at whether there may be significant relationships between fasting plasma glucose (FPG) and severity of inflammations.

All cases with the digital clubbing were included.The study included 104 cases with clubbing detected among 2.428 cases (1.044 males). So clubbing was higher in males (8.1% versus 1.3%, p<0.001). Mean age of clubbing cases was 49.2 years, and there was a male predominance (81.7%), again. Parallel to the male predominance, there were higher prevalences of smoking (69.2% versus 41.6%, p<0.001), chronic obstructive pulmonary disease (COPD) (27.8% versus 10.8%, p<0.001), and coronary heart disease (CHD) and/or peripheric artery disease (PAD) (7.6% versus 0.0%, p<0.01) in the clubbing cases. Whereas the body weight, body mass index (BMI), and FPG were lower in the clubbing cases but the differences were nonsignificant probably due to the small sample size. But diabetes mellitus (DM) (12.5% versus 21.6%, p<0.05) and systolic blood pressure (BP) (127.6 versus 136.9 mmHg, p= 0.011) were lower in the clubbing cases, significantly. The authors concluded that there are significant relationships between smoking, digital clubbing, COPD, CHD, and PAD probably due to strong atherosclerotic effects of smoking. Similarly, the body weight, BMI, FPG, systolic BP, and DM are inversely related with the clubbing probably due to the severe inflammatory effects of smoking on the vascular endothelium, again. FPG may behave as a positive acute phase reactant (APR) in mild inflammatory disorders such as irritable bowel syndrome but as a negative APR in moderate and severe inflammatory disorders such as smoking, digital clubbing, and sickle cell diseases.

Helvaci.., et al., looked whether an exaggerated capillary endothelial edema may be the cause of sudden deaths in sickle cell diseases. Sickle cell diseases (SCDs) are inborn and severe inflammatory processes on vascular endothelium, particularly at the capillaries which are the actual distributors of the sickled or just hardened red blood cells (RBCs) into the tissues. All patients of the SCDs were included. We studied 222 males and 212 females with similar ages (30.8 vs 30.3 years, p>0.05, respectively). Disseminated teeth losses (5.4% vs 1.4%, p<0.001), ileus (7.2% vs 1.4%, p<0.001), cirrhosis (8.1% vs 1.8%, p<0.001), leg ulcers (19.8% vs 7.0%, p<0.001), digital clubbing (14.8% vs 6.6%, p<0.001), coronary heart disease (18.0% vs 13.2%, p<0.05), chronic renal disease (9.9% vs 6.1%, p<0.05), chronic obstructive pulmonary disease (25.2% vs 7.0%, p<0.001), and stroke (12.1% vs 7.5%, p<0.05) were higher in males but not acute chest syndrome (2.7% vs 3.7%), pulmonary hypertension (12.6% vs 11.7), deep venous thrombosis and/or varices and/or telangiectasias (9.0% vs 6.6%), or mean age of mortality (30.2 vs 33.3 years) (p>0.05 for all). The authors concluded that the sickled or just hardened RBCs-induced capillary endothelial damage, inflammation, edema, and fibrosis are initiated at birth, and terminate with disseminated tissue hypoxia, multiorgan failures, and sudden deaths even at childhood. Although RBCs suspensions and corticosteroids in acute and aspirin plus hydroxyurea in acute and chronic phases decrease severity of the destructive process, survivals are still shortened in both genders, dramatically. Infections, medical or surgical emergencies, or emotional stresses-induced increased basal metabolic rate aggravates the sickling and capillary endothelial edema, and may terminate with multiorgan failures-induced sudden deaths in the SCDs.

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Relationship between Parenting Styles and Temper Tantrums of Bahraini Children aged 24-48 months old at Primary Care, Kingdom of Bahrain

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Abstract

Background: Temper tantrums are episodic, unmodulated displays of intense emotional distress, often characterized by outbursts of anger, and may involve aggressive or destructive behaviour. These episodes can be effectively managed through the application of evidence-based parenting strategies that are tailored to a child's individual needs and developmental stage.

Objective: This study aimed to determine the relationship between parenting styles and the temper tantrums of children aged 2-4 years old at primary care in the Kingdom of Bahrain.

Research Method: For this research a cross-sectional, descriptive study design was employed, and a non-probability convenience sampling method was utilized to recruit a sample of 400 participants, that included 8 health centres located in Bahrain (Muharraq, BBK Hidd, Jidhafs, Sitra, Hamad Kanoo, Yousef Abdulrahman Engineer, Mohammed Jassim Kanoo, and Sh. Jaber Al Ahmed Al Sabah HCs), for a duration of 3 months (May 2022 to July 2022). The analysis technique employed was the chi-square test, a statistical method that is used to examine the association between two categorical variables.

Results: The findings of this study demonstrated that more than half of the participating children exhibited temper tantrums that lasted more than 30 minutes and showed that approximately less than one-third (31%) of the children experienced weekly or daily tantrums: however, half of the parents reported that moderate tantrums were exhibited by their youngsters. The most frequently reported tantrum behaviour was "crying", followed by "screaming" or "shouting". A child's request for an item or activity was the most frequent cause, and most tantrums occurred when their parents denied this request. Children threw temper tantrums most frequently in their homes or cars. Parents' most common strategy for stopping a child's tantrums was speaking soothingly, with spanking being the least common. The results indicated that permissive parenting styles were associated with a higher frequency of temper tantrums than authoritative parenting styles.

Conclusion: The results highlight significant aspects of tantrums, such as the duration, as children managed to maintain a tantrum episode for more than seven minutes on average. Tantrum behaviours, reasons, locations, context, and parents' strategies to control tantrums were emphasized as significant for developing proper interventions. The findings highlight the importance of parental styles in the development of children and the need for further investigation in this area.

Keywords: children aged 2-4 years old, parenting style, temper tantrum.

Introduction

Temper tantrums (TT) are a common behavioural disorder in children aged 1.5-4 years old. A thorough evaluation of children's developmental, psychological, and physiological milestones is essential for identifying the underlying cause of TT [1]. There are two types of TT: classical and non-classical. Classical TT is unpleasant, exaggerated, and sometimes aggressive expression of a child's frustration or anger that are usually disproportionate to the given situation. They occur once a day for three minutes, with no injury to themselves or others, and last less than one minute [1]. Non-classical TT continue beyond the age of 4, with injury to themselves or others, lasting for more than 15 minutes and occurring more than five times a day with persistent negative mood between tantrums [2, 3].

The clinical features of TT include crying, screaming, biting, destroying property, throwing objects, or showing violence to defiance, with a child expressing their frustration due to poor developmental skills [4, 5]. Children's misbehaviour in TT results from developmental factors, intellectual processing, temperament, health status, and family learning skills acquired through reflection, imitation, and the surrounding environment [6, 7]. TT peak at 18 to 24 months, slightly decline from 30 to 36 months, and sharply decline by 59% after 42 months [8]. Overall, 21.3% of TT occur daily, 37.3% occur weekly, 30.7% occur monthly, and 10.7% occur yearly [5]. A total of 46.5% of TT last between 5 and 10 minutes [9].

The risk factors for TT are linked to either children or parental causes. Child risk factors are more common in males and include physiological triggers, disruptive disorders, behavioural disorders, adjustment disorder, anxiety, posttraumatic stress, expressive language disorder, or intellectual delay. Parental risk factors include maternal employment, child neglect/abuse, parental divorce/separation, parental distress, low-income family status, and authoritarian, permissive, and neglectful parenting styles [10-12].

TT occur as part of a regular behavioural change during preschool age and helps children achieve healthy progress in their early development with appropriate parental support and warmth [13, 14]. To prevent TT, it is crucial to teach children new skills for connecting with others by providing daily living abilities, discouraging inappropriate social interaction, encouraging them to gain autonomy, enhancing independence, establishing gender identity, developing emotional regulation, and promoting self-reflection. Role-model parents help their children develop empathy and recognize identities, feelings, and communication [15, 16]. Poor parenting behaviour and a deprived parenting style lead to children's TT [4]. If parents are flexible, loving, and compassionate in response to their children, TT will be halted [17].

Parenting style plays a crucial role in the development of children's behaviour. The authoritarian parenting style is exhibited thorough evaluation and control of a child's attitude and behaviour following rigorous standards defined by their parents. The permissive parenting style relies on acceptance and nonpunitive parenting towards the child's actions and behaviour. The neglectful parenting style is exhibited through both low demandingness and responsiveness in the form of avoiding behavioural control but setting a small number of conduct expectations. Parenting styles affect TT due to the role of parents as protectors and educators in establishing their children's character formation [10].

Temper tantrums are directly affected by five factors: family environment, parenting style, adjustment, emotional intelligence, and children's independence (29.8%, 22%, 8.68%, 7.06%, and 4.53%, respectively) [10]. An elevated level of parental care of the family environment is associated with fewer TT; in contrast, poor parental care, lack of involvement, and poor supervision are associated with antisocial behaviour such as TT [10]. Self-adjustment and emotional intelligence, which are acquired through family, social and genetic factors, maintain behavioural equilibrium and control negative thinking to develop self-regulated emotions [10]. This is the first study in Bahrain; moreover, there is a scarcity of studies on TT in Arab countries (Emirates and Jordan) [17, 19].

This study will provide parents with observed data to help them reflect on strategies and behaviours for dealing with TT. It will also provide researchers with a fundamental basis for further research to evaluate TT among Arab children and develop mediations and guidelines on how to react to children's TT. The aim of this study is to assess the TT behaviour (e.g., frequency, severity, duration, reasons, locations, context, and parent's strategies) of Bahraini children aged 24 months to 48 months old, including all children of the participant families within the stated age range, and to measure the relationship between TT and common parenting styles.

Materials and Methods

A cross-sectional, descriptive study design was used. Non-probability convenience sampling was used to recruit participants. A Sample Size of 411 participants, was estimated based on The National Education Association Research Bulletin Formula (1960). The expected (P) was set to 0.50 (50%), with a 95% confidence interval (CI) and precision of 0.05. The calculated sample size was approximately 381. The final sample size obtained was 411 participants. Parents of a child aged between 24 and 48 months old at one of 8 health centres located in Bahrain (Muharraq, BBK Hidd, Jidhafs, Sitra, Hamad Kanoo, Yousef Abdulrahman Engineer, Mohammed Jassim Kanoo, and Sh. Jaber Al Ahmed Al Sabah HCs) were invited to participate in this study. The selected health centres are open 24 hours and cover high-density catchment areas for a a duration of 3 months (May 2022 to July 2022).

Inclusion Criteria: If parents can read and write Arabic or English., If parents can provide informed consent and If parents are interested in the study.

Exclusion Criteria: If their children had poor social skills communication., If parents could not read or write Arabic or English and If parents were not interested in the study. For this study, three types of questionnaires were used; the first was used to collect sociodemographic information, the second was a 45-item tantrum questionnaire, and the third explored common parenting styles.

Sociodemographic characteristics: This questionnaire was developed based on previous research. It included eleven items: four items on children (age, sex, child order, number of children) and four items on parents (parent's age at marriage, socioeconomic status, parent's educational levels, parent's employment status). We used the categories of "younger" children aged 24–36 months old and "older" children aged >36–48 months old [20]. The parents were asked to recall their child's behaviour over the last three months and report a description of TT, types, reason, location, context, and their own coping strategies. The 45-item Tantrum Questionnaire collected parental responses using a 5-point Likert scale ranging from 0 "Never" to 4 "Always. It is a valid and reliable scale. This scale is intended to capture children's behaviour and their parent's responses during TT [5].

Moreover, the instrument is in the common domain and free to use. It was translated from its original language (English) to the target language (Arabic). The parents were asked to recall their parenting style. Then, their scores were added up and the total was divided by the number of items to find the calculated score for each category. The highest calculated score indicated each parent's preferred parenting style. Parental responses on parenting style were collected using a 6-point Likert scale ranging from 1 (never) to 6 (always).

Translation and Pilot Testing:
We used the Arabic version of the 45-item tantrum questionnaire that has been used in other studies and proved its high validity and reliability (Cronbach's alpha of 0.80) [20].

Then, we used the Arabic version in the pilot study with 20 participants who were not involved in the main study. Reliability analysis was performed to assess the internal consistency using Cronbach's alpha test, and the results indicated that Cronbach's alpha coefficients for tantrum behaviour, reasons for child's tantrums, locations of child's tantrums, context of child's tantrum behaviours, parent's strategies for stopping child's tantrums, rate your response, authoritative parenting style, and permissive parenting were 0.889, 0.852, 0.805, 0.833, 0.821, 0.905, 0.928, and 0.762, respectively.

The quantitative variables were presented as the mean and standard deviation, whereas the categorical variables were presented as frequencies and percentages. The internal consistency reliability using Cronbach's alpha coefficient were used to verify the reliability of the questionnaire. Two independent sample t tests were used to verify the significant mean differences in aspects of tantrum behaviour according to the age of the child and the severity of tantrums. One-way analysis of variance (ANOVA) was used to compare the mean aspects of tantrum behaviour for different groups. The post- hoc test using the Scheffe method was used to determine the significance of pairwise mean differences in the aspects of tantrum behaviour according to different levels. The Statistical Package for Social Sciences (SPSS), version 28 (Chicago, IL, USA), was used to analyse the collected data. Statistical significance was set at p value < 0.05.

Ethical Consideration:
After obtaining ethical approval from the primary care ethical committee, we distributed a questionnaire with a cover letter, which included the purpose and objectives of the study. After a full explanation of the study purpose, the letter included an invitation to all voluntary participants. Additionally, the voluntary participants could withdraw at any time without any consequences. All parents were asked to provide written consent and were assured that their data would remain confidential.

Results

Demographic characteristics of the participants
A total of 425 questionnaires were distributed to participants who met the inclusion criteria, and 411 participants agreed to take part. The response rate was excellent at 96.7%. The majority of the children were male (53.3%); most were at the age of 37-48 months (63%), and the mean age of the children was 3.02. Overall, 56.2% and 45.4% of the mothers and fathers, respectively, had an education level of diploma or above. Approximately 92.4% of the fathers and 51.8% of the mothers were employed, and the mean ages of the fathers and mothers were 26.5 and 22.9, respectively (Table 1). As a result, most children were first (36.0%) or second (31.3%) in the sibling order. Overall, 60.3% of the families had an income between 1000-3000 BD/monthly (Table 1).

Table 1. Sociodemographic characteristics of participants (n =411).

Characteristics	Frequency (n)	Percent (%)
Child gender		
Female	192	46.7
Male	219	53.3
Child age		
24-36 months	139	37.0
37-48 months	237	63.0
Fathers' education level		
Primary	13	3.2
Intermediate	32	7.8
Secondary	179	43.7
Diploma and above	186	45.3
Mothers' education level		
Primary	15	3.7
Intermediate	32	7.8
Secondary	132	32.3
Diploma and above	230	56.2
Fathers' occupation		
Employed	376	92.4
Unemployed	25	6.1
Others	6	1.5
Mothers' occupation		
Employed	212	51.8
Unemployed	191	46.7
Others	6	1.5
Childbirth order		
First born	145	36.0
Second born	126	31.3
Third born	107	26.6
Fourth born and beyond	25	6.1
Income		
Less than 1000	55	13.4
Between 1000-2000 BD	128	31.1
Between 2001-3000 BD	120	29.2
More than 3000 BD	108	26.3
Age	**Mean**	**St. Deviation**
Child	3.02	1.10
Father	26.53	6.03
Mother	22.89	4.49

Description of children's tantrums

More than one-third (37.8%) of the parents reported that their child had infrequent TT, while less than one-third of the TT occurred weekly or daily, with rates of 31.2% and 31%, respectively. The severity of TT, as reported by parents, was either mild (44.6%) or moderate (50.7%). The mean TT duration was 4.86 minutes, ranging between 5.0 minutes and 20.0 minutes. The most frequently reported tantrum behaviour was 'crying' (mean = 2.43, SD = 1.13; 60.8) followed by 'screaming or shouting' (mean = 2.23, SD = 1.16; 55.8%), which was the normative, distress type of TT, followed by destructive and non-destructive types, as shown in Table 2.

Table 2. Description of child's tantrum (n=411)

Description	N	%
Frequency of child tantrums in the past three months		
Daily	127	31.2
Weekly	126	31.0
Less often	154	37.8
Severity of tantrums		
Mild (Low Risk)	180	44.6
Moderate (Higher Risk)	205	50.7
Severe (Highest Risk)	19	4.7
Duration of tantrums (Minutes)		
Less than 5 minutes	170	41.4
6-10 minutes	24	5.8
11-30 minutes	6	1.5
More than 30 minutes	211	51.3
Duration of tantrums (Minutes)	**Mean, Median (IQR) = 4.86, 3 (5-2)**	
Tantrum behaviour	**Mean (SD)**	
Crying	2.43 (1.13)	60.8
Screaming or shouting	2.23 (1.16)	55.8
Hitting parents or siblings	1.23 (1.19)	30.8
Hitting objects	1.05 (1.16)	26.3
Throwing self on floor	0.98 (1.22)	24.5
Stomping feet	0.74 (1.14)	18.5
Deliberately hitting own head against something	0.41 (0.83)	10.3
Breaking things	0.74 (0.99)	18.5
Throwing things	1.11 (1.12)	27.8
Biting	0.55 (0.91)	13.8
Kicking	0.80 (1.04)	20.0

N: Frequency, %: Percentage, SD: Standard Deviation; IQR: Interquartile Range

Reasons for tantrums

Examining the related reasons of child's tantrums revealed (Table 3) that "the child's request for an item or activity (e.g., snack) was denied" was the most common reason for tantrums that parents reported (mean = 2.14, SD = 1.32; 53.5%), followed by "child was involved in the activity and did not want to start/stop/change activity" (mean=1.82, SD=1.32; 45.5%). This was followed by "the child wanted attention" (mean=1.80, SD= 1.29, 45.0%).

Table 3. Reasons for children's tantrums (N=411)

Reasons	Mean (SD)	%
Child was hungry or tired	1.59 (1.27)	39.8
Child wanted attention	1.80 (1.29)	45.0
Child was sick or in pain	1.67 (1.26)	42.8
Child's request for an item or activity (e.g., snack) was denied	2.14 (1.32)	53.5
Child was involved in the activity and did not want to start/stop/change activity (e.g., to get dressed)	1.82 (1.32)	45.5
I do not know what started it	1.47 (1.21)	36.8

SD: Standard Deviation; %: Percentage.

Locations, context, and parents' strategies

The results show that the most frequent location where children threw TT was in the home (mean=2.45, SD=1.26, 61.3), followed by in the car (mean =1.64, SD=1.09, 41.0) and public places (mean = 1.50, SD = 1.30; 37.5%). The most common context for TT was at the child's home when they were supposed to go to bed (mean = 1.37, SD = 1.15; 34.3%) and when left alone (mean=1.37, SD=1.10, 34.3%). The parents' strategies for stopping the TT included speaking soothingly to the child (mean =2.44, SD=1.34, 61%), picking the child up and holding them (mean 2.32, SD= 2.08, 58%), helping the child talk about the cause of their anger (mean=2.30, SD= 1.36, 57.5%), commanding the child to stop throwing a tantrum (mean= 2.19, SD= 1.35, 54.8%) or finding a way to distract the child (mean= 2.13, SD= 1.34, 53.3%) (Table 4).

Table 4. Sites, context, and parents' strategies for coping with children's tantrum behaviour (N=411)

Description	Mean (SD)	%
Locations of child's tantrum		
At home	2.45 (1.26)	61.3
In public places	1.50 (1.30)	37.5
In the car	1.64 (1.09)	41.0
When visiting someone else's home	1.08 (1.03)	27.0
Context of child's tantrum behaviour		
When dressing	1.12 (1.02)	28.0
At meals	1.35 (1.15)	33.8
When getting washed	1.24 (1.12)	31.0
When they were supposed to go to bed	1.37 (1.15)	34.3
When left alone	1.37 (1.10)	34.3
When in the company of other children	1.12 (1.05)	28.0
When routines changed	1.18 (1.21)	29.5
In their own home, when having guests	0.85 (1.01)	21.3
When troubled by intense sounds or lights	0.86 (1.02)	21.5
In new, unfamiliar situations	1.13 (1.25)	28.3
Parent's strategies for stopping child's tantrums		
Speaking soothingly to the child	2.44 (1.34)	61.0
Picking the child up and holding him or her	2.32 (2.08)	58.0
Commanding the child to stop	2.19 (1.35)	54.8
Stating a consequence (e.g., timeout)	1.77 (1.46)	44.3
Spanking the child	0.85 (1.19)	21.3
Ignoring the behaviour	1.46 (2.94)	36.5
Giving the child what he or she wanted	1.74 (1.97)	43.5
Offering the child a reward if he or she would behave	1.94 (1.26)	48.5
Turning their back on the child and walking away	1.42 (1.31)	35.5
Finding a way to distract that child's attention away from whatever was upsetting him or her	2.13 (1.34)	53.3
Helping the child talk about the causes of his or her anger	2.30 (1.36)	57.5

Comparison of aspects of tantrum behaviour according to the age of the child and the severity of tantrums

The study results of the independent samples t test revealed that there was no statistically significant difference in the mean of the aspects of tantrum behaviour between the younger and older children (Table 5).

Table 5. Comparison of the aspects of tantrum behaviour between younger and older children

Aspects of Tantrum Behaviour	Child's age				P. value
	Younger Children (n=118)		Older Children (n=206)		
	Mean	St. Deviation	Mean	St. Deviation	
Reason	10.61	5.55	10.49	5.55	0.852
Locations of child's tantrum	6.90	3.36	6.55	3.23	0.336
Context of child's tantrum	11.25	6.77	11.91	7.22	0.391
Parent's strategies	19.79	8.03	20.29	8.27	0.588

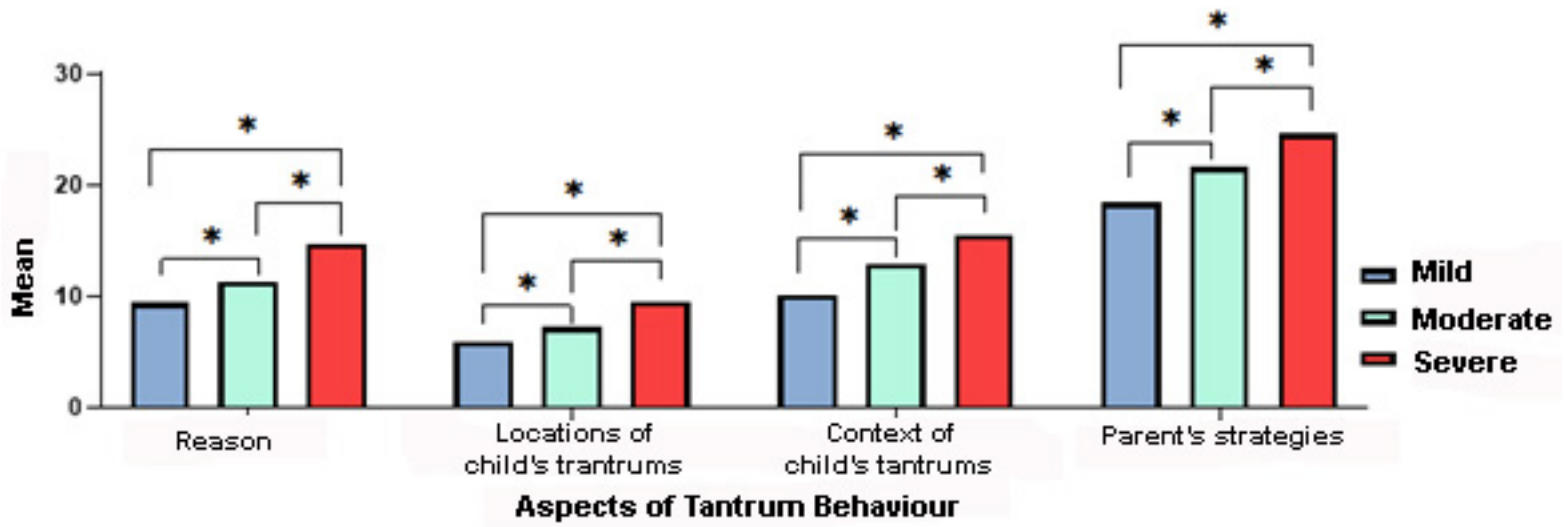
To compare the aspects of tantrum behaviour according to the level of severity of tantrums, analysis of variance (ANOVA) was conducted, and the results indicated that there were statistically significant differences in the mean of all aspects of tantrum behaviour (reason, locations of child's tantrum, context of child's tantrum, and parents' strategies) according to the level of severity of tantrums $F(2, 346)=10.753$, $p<0.001$; $F(2, 389)=15.518$, $p<0.001$; $F(2, 377)=9.689$, $p<0.001$; and $F(2, 357)=8.724$, $p<0.001$, respectively (Table 6).

Table 6. Analysis of variance to compare the aspects of tantrum behaviour according to the severity of tantrums.

Aspects of Tantrum Behaviour	Severity of tantrums			P. value
	Mild (n=156)	Moderate (n=173)	Severe (n=18)	
	Mean ± SD	Mean ± SD	Mean ± SD	
Reason	9.37 ± 5.06	11.28 ± 5.51	14.61 ± 5.61	< 0.001
Locations of child's tantrum	5.85 ± 3.25	7.18 ± 2.97	9.44 ± 4.15	< 0.001
Context of child's tantrum	10.13 ± 6.42	12.80 ± 6.87	15.53 ± 9.42	< 0.001
Parent's strategies	18.39 ± 8.25	21.57 ± 8.33	24.56 ± 7.37	< 0.001

To determine the significance of pairwise mean differences in the aspects of tantrum behaviour according to the levels of severity of tantrums, the posthoc test using the Scheffe method was employed and showed that there were statistically significant differences in the mean of all aspects of tantrum behaviour (reason, locations of child's tantrum, context of child's tantrum, and parents' strategies) between the children whose level of tantrums was severe and those whose level of tantrums was moderate, with the severe level being favoured, between severe and mild, with severe being favoured, and between moderate and mild, with moderate being favoured (Figure 1).

Figure 1. Post hoc test to compare the significance of the differences between the means of aspects of tantrum behaviour according to the severity of tantrum.



Type of parenting style:
To compare the type of parenting style according to maternal years of education, analysis of variance (ANOVA) was conducted, and the results revealed that there were statistically significant differences in the mean of democratic and permissive styles F(3, 380)=7.167, p<0.001; F(3, 223)=2.842, p=0.039, respectively (Table 7).

Table 7. Analysis of variance to compare the parenting style according to the maternal years of education

Parenting style	Mother's years of education				P. value
	Primary (n=13)	Intermediate (n=29)	Secondary (n=122)	Diploma and above (n=217)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Democratic Parenting Style	5.04 ± 0.97	3.97 ± 1.37	4.56 ± 0.98	4.66 ± 1.00	< 0.001
Authoritarian Parenting Style	2.09 ± 2.37	2.07 ± 1.38	2.02 ± 1.54	1.70 ± 1.55	0.269
Permissive Parenting Style	1.45 ± 1.66	1.72 ± 1.16	2.56 ± 1.52	2.47 ± 1.43	0.039

To determine the significance of pairwise mean differences in the type of parenting style according to the maternal years of education, the posthoc test using the Scheffe method was employed and indicated that there were statistically significant differences in the mean of the democratic parenteral style between mothers with a primary education level and an intermediate level, with primary being favoured, between secondary and intermediate level, with secondary being favoured, and between diploma and above and intermediate, with diploma and above being favoured (Figure 2). Regarding the permissive style, the results showed that there were statistically significant differences in the mean of the parenting style permissive between mothers with secondary level and primary or intermediate education level, with secondary level being favoured, and between diploma and primary or intermediate level, with diploma being favoured (Figure 3).

Figure 2. Post hoc test to compare the significance of the differences between the means of parenting styles according to the mother's years of education.

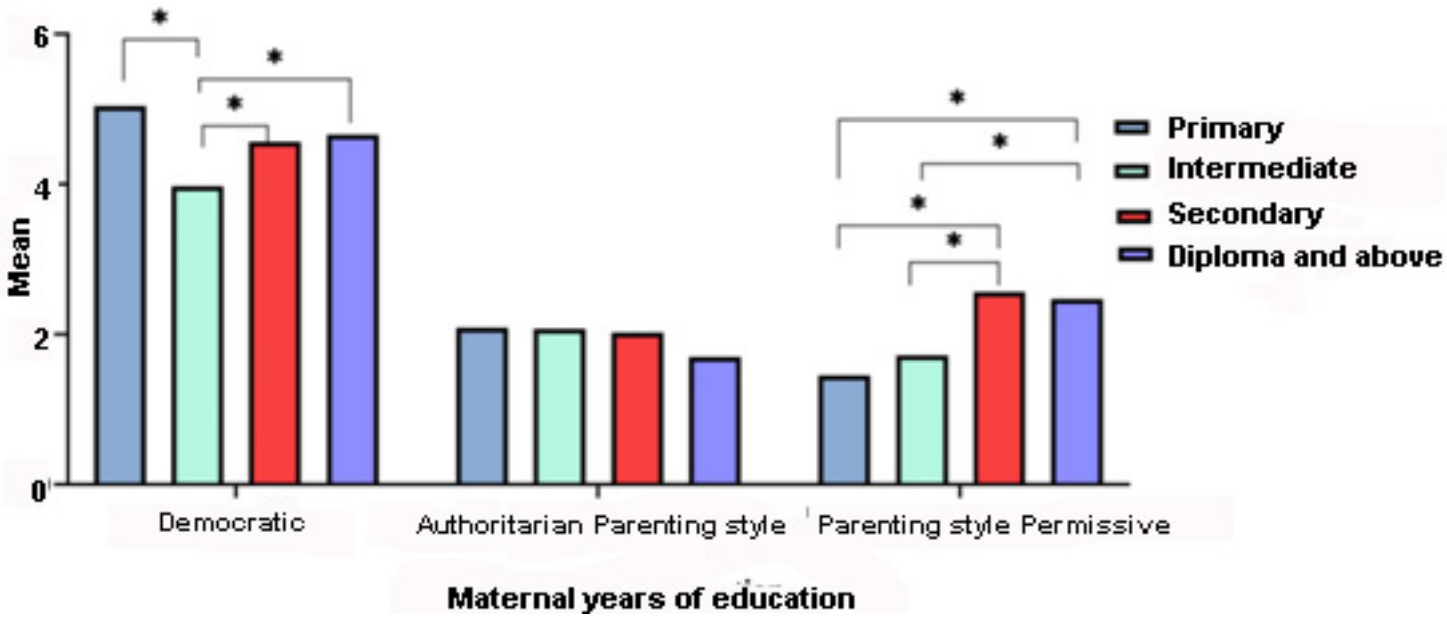
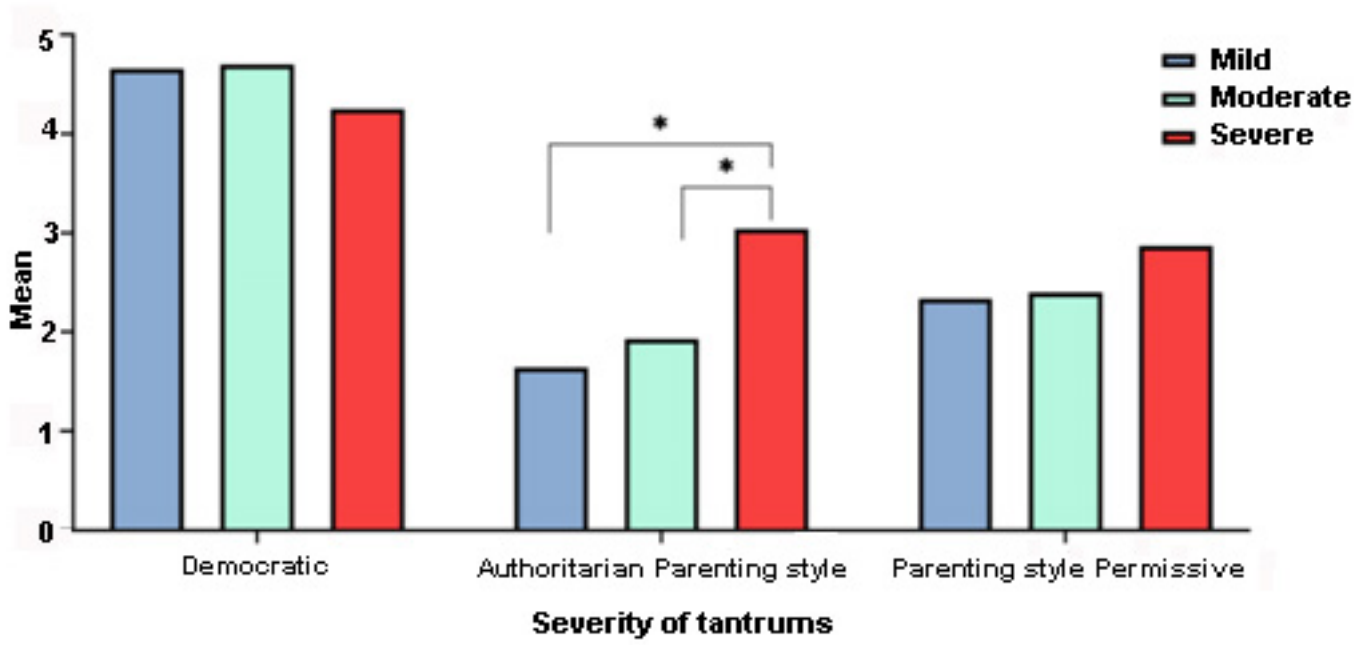


Figure 3. Post hoc test to compare the significance of the differences between the means of authoritarian parenting styles according to the severity of tantrums.



Discussion

This study aimed to investigate the relationship between parental styles and the frequency of temper tantrums and their coping strategies. Over half of the participants' children exhibited tantrums lasting more than 30 minutes, in contrast to a study in Wisconsin in which 75% of tantrums lasted 5 minutes or less [9]. Crying was the most common tantrum behaviour, with screaming and shouting being the second most common, which aligns with the findings of a study conducted in Jordan [20].

Our study found that the most common cause of tantrums was the denial of a child's request for an item or activity, which is consistent with a study conducted at the University of Connecticut [21]. This finding contrasts with the statement in "Essentials of Pediatric Nursing" that hunger and attention seeking are the most common reasons [22]. Tantrums most commonly occurred at home and least frequently in someone else's house, which corresponds to another study [21]. Speaking soothingly to the child was the most common parental strategy for stopping tantrums, while spanking was the least common, consistent with a published guideline article [23].

The topic of children's temper tantrums and the impact of parental styles on their occurrence is of significant interest in the field of child development and psychology. Our study revealed a significant association between parental styles and the frequency of children's temper tantrums. Permissive parenting styles were associated with a higher frequency of temper tantrums compared to authoritative parenting styles, consistent with previous research [24, 25]. Chen et al. also found a negative relationship between parental control and temper tantrums in preschool-aged children, while parental warmth was positively related to temper tantrums [26]. Kim et al. found that parental stress is associated with an increased frequency of children's temper tantrums [27]. This is important, as permissive parenting styles have been linked to higher levels of parental stress [28].

The strength of medical research on the relationship between parental style and children's temper tantrums lies in identifying specific behaviours and attitudes that contribute to the problem and inform the development of more effective interventions. However, this research may not fully capture the complexity of the relationship between parental style and children's temper tantrums due to other factors, such as genetics or environmental factors, which also play a role. Small sample sizes or other limitations may affect the generalizability of some studies to the broader population.

Our results contribute to the growing body of literature that suggests a link between parental styles and the frequency of children's temper tantrums. The findings highlight the importance of parental styles in the development of children and the need for further investigation in this area. By identifying the factors that contribute to the development of temper tantrums, research can inform the development of more effective interventions for children with temper tantrums and improve their well-being.

In conclusion, this study found a significant association between parental styles and the frequency of children's temper tantrums, consistent with previous research. Our results highlight the importance of investigating parental styles in connection to the development of children and inform the development of more effective interventions for temper tantrums.

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The prevalence of Hypertension among patients with hyperlipidemia in Imam Muhammed Ibn Saud Islamic University medical center

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Abstract

Background: The prevalence of cardiovascular diseases and their complications is rising, and they are considered the leading reason of death, along with disability, in many nations (1). Among the other cardiovascular risk factors, hypertension and dyslipidemia play a crucial role in developing various disorders, but most importantly, cardiovascular diseases (2), (3).

Aim: To measure the prevalence of hypertension among hyperlipidemic patients at Imam Mohammad Ibn Saud Islamic University (IMSIU) medical center. Additionally, we set out to measure the prevalence of diabetes mellitus among the same sample.

Methods: The present study is an observational retrospective study that includes collecting data from medical records in a cardiology clinic from 16/03/2017 to 25/04/2021 at the IMSIU medical center in Riyadh, Saudi Arabia.

Results: There were 413 subjects in total who took part in the investigation, with males constituting 85.7% of the sample. In addition, 83.1% of the patients were over the age of 40. It was recognized that among patients with hyperlipidemia, hypertension was reported in 60.1% of them. Also, 58.7% of patients with hyperlipidemia have diabetes mellitus. Regarding prescriptions, 75.1% of the patients were on lipid-lowering medications. Besides, it was noticed that the prevalence of diabetes mellitus and hypertension rose dramatically with age.

Conclusion: It was revealed that most patients with hyperlipidemia also have concurrent hypertension. On top of that, most hyperlipidemic patients are diagnosed with diabetes mellitus. Overall, the main findings support previous studies' results that suggest an association between hyperlipidemia and hypertension.

Keywords: Hypertension; Hyperlipidemia; Diabetes Mellitus.

Introduction

Cardiovascular disease (CVD), which includes coronary heart disease, cerebrovascular diseases, and peripheral arterial disease, is recognized as one of the main causes of mortality worldwide (4). The prevalence of cardiovascular diseases and their complications is rising, and they are the leading cause of death along with disability in many countries, which makes it a critical topic to focus on (5). A global study estimated that 17.92 million deaths occur annually due to CVDs (5). This large number of cases indicates the need for appropriate management, recognizing risk factors, and prevention of CVDs. The risk factors of cardiovascular disease (CVD) are well-known as they include lipid disorders, hypertension, tobacco smoking, obesity, diabetes, male gender, and physical inactivity. Of these factors, hypertension and dyslipidemia play a crucial role in developing various disorders, but most importantly, cardiovascular diseases (2). A significant proportion of the population is diagnosed with dyslipidemia and hypertension, which, as mentioned, are risk factors for cardiovascular diseases (5). Dyslipidemia, which includes increased levels of cholesterol, low-density lipoprotein cholesterol, triglycerides, and low levels of high-density lipoprotein cholesterol in the circulating blood, is a major risk factor for atherosclerosis that leads to various cardiovascular diseases (6). In addition, the association between hypertension and dyslipidemia is common, which may be due to a shared pathogenesis between the two conditions (7). A systematic review conducted in GCC countries showed that hypertension prevalence was 26% to 50.7% in males and 20.9% to 31.7% in females (8). Dyslipidemia has a considerable impact on the body's blood pressure, which has an important role when addressing cardiovascular diseases. Consequently, there is clear evidence that hyperlipidemia and hypertension are somewhat correlated in terms of epidemiological statistics, metabolic processes, and clinical features (9), (10). Besides, having both of these major risk factors for cardiovascular disease—hypertension and hyperlipidemia—may increase the risk of developing CVD more than either risk factor alone (11). The co-existence of hypertension and hyperlipidemia with the mechanism by which these two come into line remains not sufficiently understood. This vagueness encourages researchers to investigate more about the CVD risk factors, which is what the present study aims to do. Furthermore, hyperlipidemia and hypertension may have some overlap in underlying causes. Knowing these causes is a great help in taking appropriate therapeutic measures. As there is a scarcity of studies that are concerned with the prevalence of concomitant hypertension and hyperlipidemia, this study was performed at the Imam Mohammad Ibn Saud Islamic University medical center, precisely at the Cardiology clinic department. With regard to the objectives, the study is intended to measure the prevalence of hypertension among hyperlipidemic patients at Al-Imam Muhammed Ibn Saud Islamic University Medical Center in Riyadh, Saudi Arabia. Also, as a secondary objective, the study measured the prevalence of diabetes among patients with hyperlipidemia at the same medical center. Also, the research is planned to facilitate future epidemiological studies that intend to measure the prevalence of concomitant hypertension and hyperlipidemia on a larger scale in Saudi Arabia through systematic review or meta-analysis, which would give a more accurate idea regarding the percentage of hyperlipidemia that is accompanied by hypertension in adult patients. The motives for conducting such research are multiple and are as follows: First, the increased need for more attention as the effect of hypertension among hyperlipidemic patients may have serious consequences. Next, due to a shortage of similar studies conducted in the capital city of Riyadh, the research hypothesized that there is a high prevalence of hypertension among hyperlipidemic patients at the Imam Mohammad Ibn Saud Islamic University medical center in Riyadh, Saudi Arabia.

Methods

Following written consent that was obtained from Imam Mohammad Ibn Saud Islamic University's medical center and institutional review board approval, the research team conducted an observational retrospective study for adult patients diagnosed with hyperlipidemia who were aged 18 years old and above. Data was obtained from the medical records in Imam Mohammad Ibn Saud Islamic University medical center's database at a single cardiology clinic from 16/03/2017 to 25/04/2021. During the data collection process, patients who were aged under 18 years old and those who were not diagnosed with hyperlipidemia were excluded. There were a total of 413 individuals who matched the inclusion criteria. Once patients were selected, the present research collected and measured the following variables: demographic characteristics (gender and age), medical history (hyperlipidemia, hypertension, and diabetes mellitus), and drug profile (lipid-lowering drugs and anti-diabetic drugs). Also, the main purpose of the present study is to find out how common hypertension is among people who have a confirmed diagnosis of hyperlipidemia.

Statistical analysis

For data analysis, MS Excel was utilized, and for data analysis, SPSS version 25 was implemented. Categorical variables were delineated using frequency as well as percentage. The Chi square test was used to assess the relationship between the incidence of hypertension and diabetes mellitus and demographic characteristics such as age, gender, DM incidence, and usage of lipid-lowering medicines. Lastly, the findings revealed were significant if the p value was lower than or equal to 0.05.

Results

In the present study, data was collected on 413 hyperlipidemic patients admitted to the IMSIU medical center in Riyadh, Saudi Arabia, from 16/03/2017 to 25/04/2021. According to the findings, 85.7% of the patients were male, with a male-to-female ratio of 6:1. Regarding the age groups of the patients, it was found that 28.4% were between the ages of 51 and 60, and 26.2% were between the ages of 41 and 50. In general, 83.1% of the patients were over the age of 40, and 77.1% were between the ages of 41 and 70 (Table 1).

Moreover, it was recognized that among patients with hyperlipidemia, hypertension was reported in 60.1% of them (248 patients) (Figure 1). Additionally, it was noticed that 58.7% of those with hyperlipidemia also had diabetes mellitus. On top of that, it was found that 75.1% of the patients were on lipid-lowering medications, and 38.6% were on anti-diabetic medications (Figure 2).

Furthermore, the researchers attempted to investigate the prevalence of hypertension and diabetes mellitus in hyperlipidemic patients. The gender of the patients had a significant impact on the prevalence of hypertension and diabetes mellitus, with the prevalence of hypertension and diabetes mellitus being higher in the female population than the male population (67.8% vs. 58.8%, and 44.1% vs. 40.90%, respectively). However, the limited number of females in the present study may reduce the accuracy of this impact. Regarding the age group, it was revealed that the prevalence of hypertension and diabetes mellitus increased significantly with age, with the prevalence of hypertension increasing from 15% in patients aged 18–30 years old to 74.2% in patients aged 61–70 years old, 89.5% in patients aged 71–80 years old, and 100% in patients aged over 80 years old (P = 0.000). The same was observed when the prevalence of diabetes mellitus increased from 0% in participants aged 18–30 years old to 52.6% in patients aged 71–80 years old. Furthermore, it was discovered that there is a significant relationship between diabetes and hypertension, with 67.8% of patients with diabetes mellitus having hypertension (0.007). Finally, the prevalence of hypertension and diabetes turned out to be significantly higher in patients who were on lipid-lowering drugs in the sample (Table 2).

Table 1: The demographic factors of patients with hyperlipidemia (N=413)

		Count	Column N %
Gender	Male	354	85.7%
	Female	59	14.3%
Age	18-30	20	4.8%
	31-40	50	12.1%
	41-50	108	26.2%
	51-60	117	28.4%
	61-70	93	22.5%
	71-80	19	4.6%
	81-90	6	1.4%

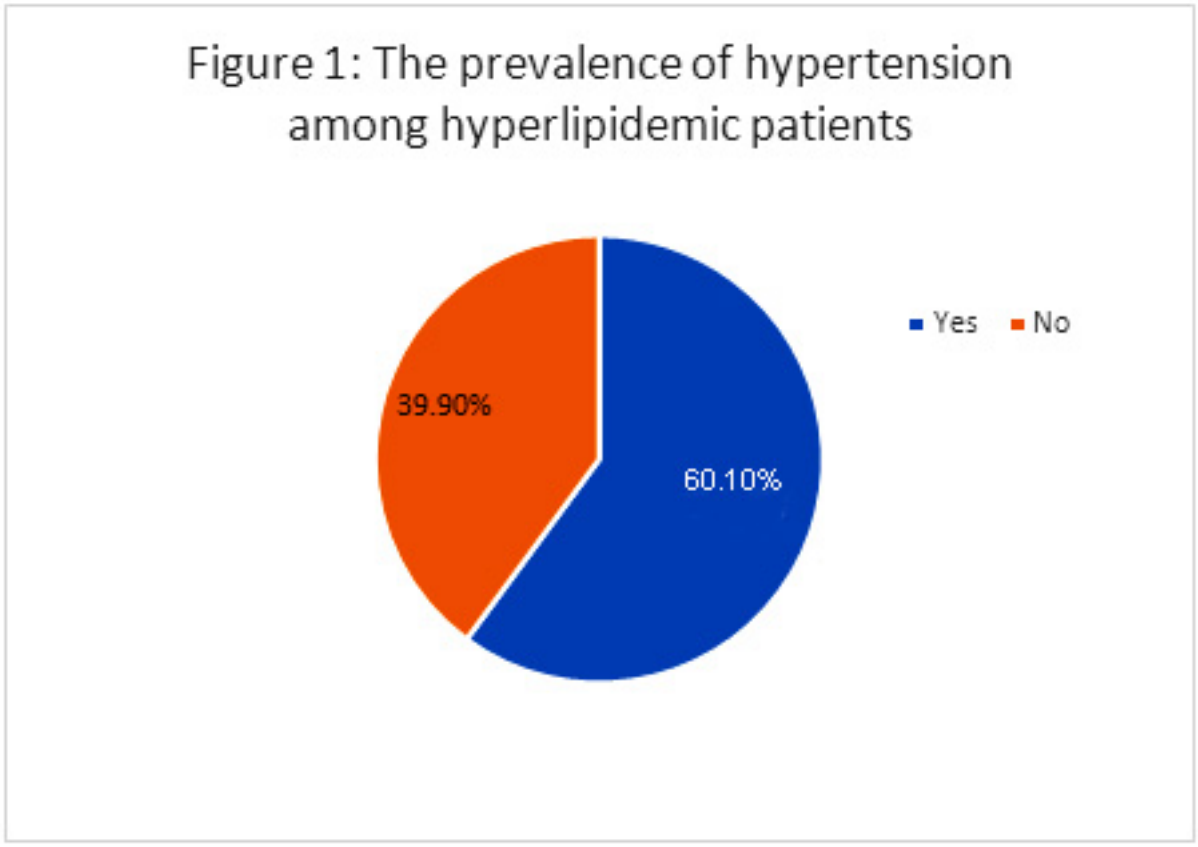
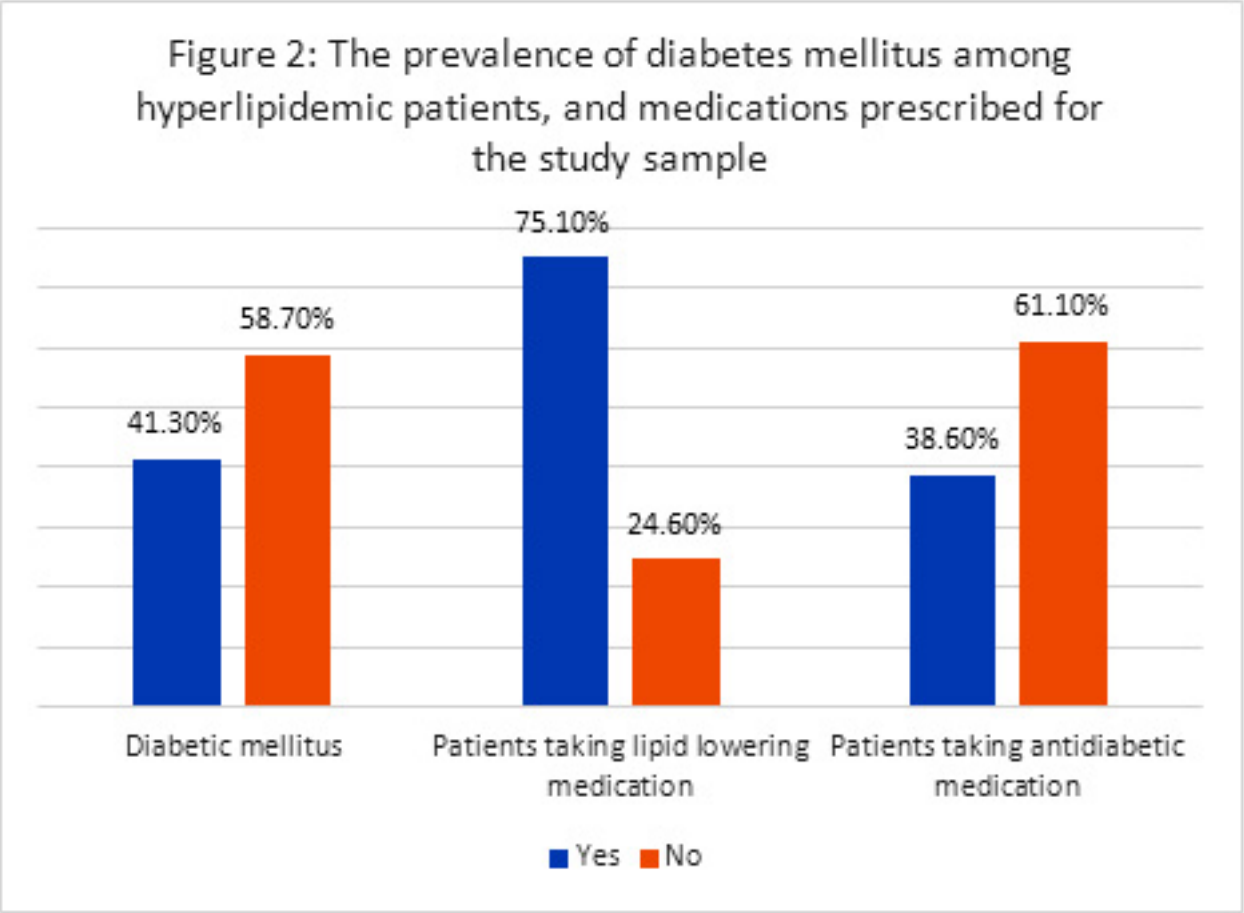


Table 2: The relation between prevalence of hypertension and diabetes mellitus and the demographic factors of hyperlipidemic patients

		Hypertension				Diabetes mellitus			
		No		Yes		No		Yes	
		Count	N %	Count	N %	Count	N %	Count	N %
Gender	Male	146	41.2%	208	58.8%	209	59.1%	145	40.9%
	Female	19	32.2%	40	67.8%	33	55.9%	26	44.1%
	P-value	0.008*				0.012*			
Age	18-30	17	85.0%	3	15.0%	20	100.0%	0	0.0%
	31-40	33	66.0%	17	34.0%	38	76.0%	12	24.0%
	41-50	49	45.4%	59	54.6%	68	62.9%	40	37.1%
	51-60	39	33.3%	78	66.7%	58	49.6%	59	50.4%
	61-70	24	25.8%	69	74.2%	45	48.4%	48	51.6%
	71-80	2	10.5%	17	89.5%	9	47.4%	10	52.6%
	81-90	0	0.0%	6	100.0%	4	66.7%	2	33.3%
	P-value	0.000*				0.000*			
Diabetes mellitus	No	109	45.0%	133	55.0%				
	Yes	55	32.2%	116	67.8%				
	P-value	0.007*							
Taking lipid lowering drugs	No	52	51.5%	49	48.5%	83	82.2%	18	17.8%
	Yes	111	35.7%	200	64.3%	159	51.1%	152	48.9%
	P-value	0.004*				0.000*			

* Significant at p value lower or equal to 0.05.



Discussion

The study's goal was to find out how common hypertension and diabetes mellitus are among hyperlipidemic patients at IMSIU Medical Center, with hypertension being the primary aim of the investigation. In the present study's investigation, hypertension was noticed to be prevalent in 60.1% of hyperlipidemic individuals. Alzahrani G, et al. discovered a 71.8 percent prevalence of hypertension among hyperlipidemic individuals in previous research (4). When compared to earlier studies that looked at the prevalence of hypertension in the general population, this study showed that it is much greater. Another study by Bcheraoui C et al. intended to determine the prevalence of hypertension in Saudi Arabia's general population, and the results revealed a prevalence of 15.2 percent (5), while another study by Tohme R. found a prevalence of 23.1 percent (6). Other studies have established a link between a high incidence of hypertension and the occurrence of hyperlipidemia (7), (12), (13), (14), (15). One hypothesis for why hyperlipidemia is linked to the occurrence of hypertension is the influence of hyperlipidemia on the reduction of nitric oxide (NO), a vasodilator (16), as well as the link between hyperlipidemia and increased vasoconstrictor molecule release as a result of activation of the renin-angiotensin-aldosterone pathway (17).

Considering the prevalence of diabetes mellitus among hyperlipidemic patients, this study reported a prevalence of 41.3%. With respect to diabetes mellitus prevalence, it was recognized to be 59.2 percent in Alzahrani G, et al.'s study (4). In comparison with other reports, the prevalence of diabetes mellitus among the general population was found to be (12.1%) (18)–23.7%) (19), whereas this study showed that the prevalence of diabetes mellitus among the hyperlipidemic population was much higher. The relation between hyperlipidemia and diabetes mellitus might be because of the role of lipoprotein lipases, which are responsible for lipid breakdown and are controlled by insulin concentration (20). Moreover, the findings revealed that hypertension and diabetes mellitus are significantly more prevalent in the elderly population. These results confirm the results published in previous studies [1,3,5]. Furthermore, the study shows that there is a significant relationship between the incidence of hypertension and diabetes mellitus, which is supported by previous studies (21) (22) (23). The incidence of hyperglycemia and resistance-induced hyperinsulinemia is associated with increasing peripheral artery resistance, vascular remodeling, and increased body fluid volume, which are associated with increased blood pressure, inducing hypertension (22).

Limitations

Concerning the limitations, there were a set of limitations to the present investigation that were identified. One of these disadvantages is the reliance on data from a single institution. As a result, the findings could not be extrapolated to the populations of Riyadh or the Kingdom of Saudi Arabia. Consequently, it's highly encouraged that a larger-scale cohort investigation or multicenter research be conducted. In addition, female sex involvement constitutes only 14.3% of the whole sample.

Conclusion

It was revealed that most patients with hyperlipidemia also have concurrent hypertension. On top of that, most hyperlipidemic patients are diagnosed with diabetes mellitus. Overall, the main findings of the present study support previous studies' results that suggest an association between hyperlipidemia and hypertension.

Declaration of Interests: the authors declare they have no conflict of interest.

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Statement of Ethics: Ethical approval for this study's conduction and data collection was reviewed and approved by the Institutional Review Board (IRB) committee of Imam Mohammad Ibn Saud Islamic University. Written informed consent was obtained from all participants.

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An exaggerated capillary endothelial edema may be the cause of sudden deaths in sickle cell diseases

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Abstract

Background: Sickle cell diseases (SCDs) are inborn and severe inflammatory processes on vascular endothelium, particularly at the capillaries which are the actual distributors of the sickled or just hardened red blood cells (RBCs) into the tissues.

Methods: All patients of the SCDs were included.

Results: We studied 222 males and 212 females with similar ages (30.8 vs 30.3 years, p>0.05, respectively). Disseminated teeth losses (5.4% vs 1.4%, p<0.001), ileus (7.2% vs 1.4%, p<0.001), cirrhosis (8.1% vs 1.8%, p<0.001), leg ulcers (19.8% vs 7.0%, p<0.001), digital clubbing (14.8% vs 6.6%, p<0.001), coronary heart disease (18.0% vs 13.2%, p<0.05), chronic renal disease (9.9% vs 6.1%, p<0.05), chronic obstructive pulmonary disease (25.2% vs 7.0%, p<0.001), and stroke (12.1% vs 7.5%, p<0.05) were higher in males but not acute chest syndrome (2.7% vs 3.7%), pulmonary hypertension (12.6% vs 11.7), deep venous thrombosis and/or varices and/or telangiectasias (9.0% vs 6.6%), or mean age of mortality (30.2 vs 33.3 years) (p>0.05 for all).

Conclusion: The sickled or just hardened RBCs-induced capillary endothelial damage, inflammation, edema, and fibrosis are initiated at birth, and terminate with disseminated tissue hypoxia, multiorgan failures, and sudden deaths even at childhood. Although RBCs suspensions and corticosteroids in acute and aspirin plus hydroxyurea in acute and chronic phases decrease severity of the destructive process, survivals are still shortened in both genders, dramatically. Infections, medical or surgical emergencies, or emotional stresses-induced increased basal metabolic rate aggravates the sickling and capillary endothelial edema, and may terminate with multiorgan failures-induced sudden deaths in the SCDs.

Key words: Sickle cell diseases, sickled or just hardened red blood cells, capillary endothelial damage, exaggerated capillary endothelial edema, sudden deaths

Introduction

Chronic endothelial damage may be the main underlying cause of aging and death by causing end-organ failures (1). Much higher blood pressures (BPs) of the afferent vasculature may be the chief accelerating factor by causing recurrent injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the destructive process. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Due to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic natures which eventually reduce blood flow to the terminal organs, and increase systolic and decrease diastolic BPs further. Some of the well-known accelerating factors of the harmful process are physical inactivity, sedentary lifestyle, animal-rich diet, smoking, alcohol, overweight, chronic inflammations, prolonged infections, and cancers for the development of terminal consequences including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), stroke, peripheric artery disease (PAD), mesenteric ischemia, osteoporosis, dementia, early aging, and premature death (2, 3). Although early withdrawal of the accelerating factors can delay terminal consequences, after development of obesity, HT, DM, cirrhosis, COPD, CRD, CHD, stroke, PAD, mesenteric ischemia, osteoporosis, aging, and dementia-like end-organ insufficiencies, the endothelial changes cannot be reversed due to their fibrotic natures, completely. The accelerating factors and terminal consequences of the harmful process are researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in the literature (4-6). On the other hand, sickle cell diseases (SCDs) are inborn and severe inflammatory and highly destructive processes on vascular endothelium, initiated at birth and terminated with an advanced atherosclerosis-induced end-organ failures in much earlier ages of life (7, 8). Hemoglobin S causes loss of elastic and biconcave disc shaped structures of red blood cells (RBCs). Probably loss of elasticity instead of shape is the major problem because sickling is rare in peripheric blood samples of the patients with associated thalassemia minors (TMs), and human survival is not affected in hereditary spherocytosis or elliptocytosis. Loss of elasticity is present even at birth, but exaggerated with inflammations, infections, and emotional stresses of the body. The sickled or just hardened RBCs-induced chronic endothelial damage, inflammation, edema, and fibrosis terminate with disseminated tissue hypoxia all over the body (9). As a difference from other causes of chronic endothelial damage, SCDs keep vascular endothelium particularly at the capillaries which are the actual distributors of the sickled or just hardened RBCs into the tissues (10, 11). The sickled or just hardened RBCs-induced chronic endothelial damage builds up an advanced atherosclerosis in much earlier ages of life. Vascular narrowings and occlusions-induced tissue ischemia and end-organ failures are the terminal results, so the life expectancy is decreased by 25 to 30 years for both genders in the SCDs (8).

Material and Methods

The clinical study was performed in Medical Faculty of the Mustafa Kemal University between March 2007 and June 2016. All patients of the SCDs were included. The SCDs are diagnosed with the hemoglobin electrophoresis performed by means of high performance liquid chromatography (HPLC). Smoking and alcohol habits, acute painful crises per year, transfused units of RBCs in their lives, leg ulcers, stroke, surgical operations, deep venous thrombosis (DVT), epilepsy, and priapism were learnt. Cases with a history of one pack-year were accepted as smokers, and one drink-year were accepted as drinkers. A complete physical examination was performed by the Same Internist, and patients with disseminated teeth losses (<20 teeth present) were detected. Patients with an acute painful crisis or any other inflammatory process were treated at first, and the laboratory tests and clinical measurements were performed on the silent phase. A check up procedure including serum iron, iron binding capacity, ferritin, creatinine, liver function tests, markers of hepatitis viruses A, B, and C, marker of human immunodeficiency virus, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves, and to measure systolic BPs of pulmonary artery, an abdominal ultrasonography, a venous Doppler ultrasonography of the lower limbs, a computed tomography (CT) of brain, and a magnetic resonance imaging (MRI) of hips was performed. Other bones for avascular necrosis were scanned according to the patients' complaints. So avascular necrosis of bones was diagnosed via MRI (12). Associated TMs were detected with serum iron, iron binding capacity, ferritin, and hemoglobin electrophoresis performed via HPLC, becuase the SCDs with associated TMs show a milder clinic than the sickle cell anemia (SCA) (Hb SS) alone (13). Systolic BPs of the pulmonary artery of 40 mmHg or higher are accepted as pulmonary hypertension (PHT) (14). The criterion for diagnosis of COPD is a post-bronchodilator forced expiratory volume in one second/forced vital capacity of lower than 70% (15). Acute chest syndrome (ACS) is diagnosed clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum, dyspnea, or hypoxia (16). An x-ray film of abdomen in upright position was taken in patients with abdominal distention or discomfort, vomiting, obstipation, or lack of bowel movement, and ileus is diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity. CRD is diagnosed with a persistent serum creatinine level of 1.3 mg/dL or greater in males and 1.2 mg/dL or greater in females. Cirrhosis is diagnosed with physical examination, laboratory parameters, and ultrasonographic findings. Clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter of greater than 1.0, and with the presence of Schamroth's sign (17, 18). An exercise electrocardiogram is performed in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is performed for the cases with exercise electrocardiogram positivity. So CHD is diagnosed either angiographically or with the Doppler echocardiographic findings as movement disorders in the cardiac walls. Rheumatic heart disease

is diagnosed with the echocardiographic findings, too. Stroke is diagnosed by the CT. Sickle cell retinopathy is diagnosed with ophthalmologic examination in cases with visual complaints. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were the methods of statistical analyses.

Results

The study included 222 males and 212 females with similar ages (30.8 vs 30.3 years, p>0.05, respectively). Prevalences of associated TMs were similar in both genders, too (72.5% vs 67.9%, p>0.05, respectively). Smoking (23.8% vs 6.1%) and alcohol (4.9% vs 0.4%) were higher in males (p<0.001 for both) (Table 1). Transfused units of RBCs in their lives (48.1 vs 28.5, p=0.000), disseminated teeth losses (5.4% vs 1.4%, p<0.001), ileus (7.2% vs 1.4%, p<0.001), cirrhosis (8.1% vs 1.8%, p<0.001), leg ulcers (19.8% vs 7.0%, p<0.001), clubbing (14.8% vs 6.6%, p<0.001), CHD (18.0% vs 13.2%, p<0.05), CRD (9.9% vs 6.1%, p<0.05), COPD (25.2% vs 7.0%, p<0.001), and stroke (12.1% vs 7.5%, p<0.05) were higher in males but not ACS (2.7% vs 3.7%), PHT (12.6% vs 11.7), DVT and/or varices and/or telangiectasias (9.0% vs 6.6%), or mean age of mortality (30.2 vs 33.3 years) (p>0.05 for all) (Table 2). Beside that the mean ages of terminal consequences were shown in Table 3.

Table 1: Characteristic features of the study patients

Variables	Males with SCDs*	*p*-value	Females with SCDs
Prevalence	51.1% (222)	Ns†	48.8% (212)
Mean age (year)	30.8 ± 10.0 (5-58)	Ns	30.3 ± 9.9 (8-59)
Associated TMs‡	72.5% (161)	Ns	67.9% (144)
Smoking	***23.8% (53)***	***<0.001***	***6.1% (13)***
Alcoholism	***4.9% (11)***	***<0.001***	***0.4% (1)***

*Sickle cell diseases †Nonsignificant (p>0.05) ‡Thalassemia minor

Table 3: Mean ages of the consequences of the sickle cell diseases

*Acute chest syndrome †Chronic obstructive pulmonary disease ‡Pulmonary hypertension §Coronary heart disease ¶Deep venous thrombosis **Chronic renal disease

Discussion

Acute painful crises are the most disabling symptoms of the SCDs. Although some authors reported that pain itself may not be life threatening directly, infections, medical or surgical emergencies, or emotional stresses are the most common precipitating factors of the crises (19). Although the sickled or just hardened RBCs-induced capillary endothelial damage, inflammation, and edema are present even at birth, the increased basal metabolic rate during such stresses aggravates the sickling and capillary endothelial damage, inflammation, and edema, and may terminate with disseminated tissue hypoxia and multiorgan failures-induced sudden deaths in the SCDs. So the risk of mortality is much higher during the crises. Actually, each crisis may complicate with the following crises by leaving some sequelaes on the capillary endothelial system all over the body. After a period of time, the sequelaes may terminate with sudden end-organ failures and death during a final acute painful crisis that may even be silent, clinically. Similarly, after a 20-year experience on such patients, the deaths seem sudden and unexpected events in the SCDs. Unfortunately, most of the deaths develop just after the hospital admission, and majority of such cases are without hydroxyurea therapy (20). Rapid RBCs supports are usually life-saving for such patients, although preparation of RBCs units for transfusion usually takes time. Beside that RBCs supports in emergencies become much more difficult in such terminal patients due to the repeated transfusions-induced blood group mismatch. Actually, transfusion of each unit of RBCs complicates the following transfusions by means of the blood subgroup mismacth. Due to the significant efficacy of hydroxyurea therapy, RBCs transfusions should be kept just for acute events and emergencies in the SCDs (21). According to our experiences, simple and repeated transfusions are superior to RBCs exchange in the SCDs (22). First of all, preparation of one or two units of RBCs suspensions in each time rather than preparation of six units or higher provides time to clinicians to prepare more units by preventing sudden death of such high-risk cases. Secondly, transfusions of one or two units of RBCs suspensions in each time decrease the severity of pain and relax anxiety of the patients and their relatives because RBCs transfusions probably have the strongest analgesic effects during such crises. Actually, the decreased severity of pain by transfusions also indicates the decreased severity of inflammation in whole body. Thirdly, transfusions of lesser units of RBCs suspensions in each time by means of the simple transfusions decrease transfusions-related complications including infections, iron overload, and blood group mismatch. Fourthly, transfusions of RBCs suspensions in the secondary health centers prevent some deaths developed during the transport to the tertiary centers for the exchange. Finally, cost of the simple and repeated transfusions on insurance system is much lower than the exchange that needs trained staff and additional devices. On the other hand, pain is the result of complex

and poorly understood interactions between RBCs, white blood cells (WBCs), platelets (PLTs), and endothelial cells, yet. Whether leukocytosis contributes to the pathogenesis by releasing cytotoxic enzymes is unknown. The adverse actions of WBCs on the capillary endothelium are of particular interest with regard to the cerebrovascular diseases in the SCDs. For instance, leukocytosis even in the absence of an infection was an independent predictor of the severity of the SCDs, and it was associated with the higher risk of stroke (23). Disseminated tissue hypoxia, releasing of inflammatory mediators, bone infarctions, and activation of afferent nerves may take role in the pathophysiology of the intolerable pain. Because of the severity of pain, narcotic analgesics are usually required to control them (24), but according to our long term experience, simple and repeated RBCs transfusions are much more effective than the narcotics to control the intolerable pain in the SCDs.

Hydroxyurea is the first drug that was approved by Food and Drug Administration in the SCDs (25). It is an orally-administered, cheap, safe, and effective drug, and it may be the only life-saving drug in the treatment of the SCDs (26, 27). It interferes with the cell division by blocking the formation of deoxyribonucleotides via inhibition of ribonucleotide reductase. The deoxyribonucleotides are the building blocks of DNA. Hydroxyurea mainly affects hyperproliferating cells. Although the action way of hydroxyurea is thought to be the increase in gamma-globin synthesis for fetal hemoglobin (Hb F), its main action may be the prevention of leukocytosis and thrombocytosis by blocking the DNA synthesis (28, 29). By this way, the inborn inflammatory and destructive process of the SCDs is suppressed with some extent. Due to the same action way, hydroxyurea is also used in moderate and severe psoriasis to suppress hyperproliferating skin cells. As also seen in the viral hepatitis cases, although presence of a continuous damage of sickled or just hardened RBCs on the capillary endothelium, the severity of destructive process may be exaggerated by the patients' own WBCs and PLTs. So suppression of proliferation of the WBCs and PLTs may limit the capillary endothelial damage, inflammation, edema, tissue ischemia, and end-organ failures in the body (30). Similarly, final Hb F levels in the hydroxyurea users did not differ from their pretreatment levels (31). The Multicenter Study of Hydroxyurea (MSH) studied 299 severely affected adults with the SCA, and compared the results of patients treated with hydroxyurea or placebo (32). The study particularly researched effects of hydroxyurea on the painful crises, ACS, and requirement of RBCs transfusion. The outcomes were so overwhelming in the favour of hydroxyurea that the study was terminated after 22 months, and hydroxyurea was started for all patients. The MSH also demonstrated that patients treated with hydroxyurea had a 44% decrease in hospitalizations (32). In multivariable analyses, there was a strong and independent association of lower neutrophil counts with the lower crisis rates (32). But this study was performed just in severe SCA cases alone, and the rate of painful crises was decreased from 4.5 to 2.5 per year (32). Whereas we used all subtypes of the SCDs with all clinical severity, and the rate of painful crises was decreased from 10.3 to 1.7 per year ($p<0.000$) with an additional decreased severity of them (7.8/10 vs 2.2/10, $p<0.000$) (27). Parallel to our results, adults using hydroxyurea therapy for frequent painful crises appear to have a reduced mortality rate after a 9-year follow-up period (33). Although the underlying disease severity remains critical to determine prognosis, hydroxyurea may also decrease severity of the SCDs and prolong survival (33). The complications start to be seen even in infancy in the SCDs. For instance, infants with lower hemoglobin values were more likely to have higher incidences of clinical events such as ACS, acute painful crises, and lower neuropsychological scores, and hydroxyurea reduced the incidences of them (34). Hydroxyurea therapy in early years of life may improve growth, and prevent end-organ failures. Transfusion programmes can also reduce all of the complications, but transfusions carry many risks including infections, iron overload, and development of allo-antibodies causing subsequent transfusions difficult. On the other hand, elevations of liver enzymes during some acute painful crises cannot be reversed by withdrawing of the hydroxyurea therapy alone, instead withdrawal of all of the medications were highy effective in such cases during the 20-year experience on such patients. After normalization of the liver enzymes, the essential medications must be started one by one, instead of all of them at the same time, again. Thus hydroxyurea must even be used during the acute painful crises. Additionally, we observed mild, moderate, or even severe bone marrow suppressions and pancytopenia in some patients using high-dose hydroxyurea (35 mg/kg/day). Interestingly, such cases were completely silent other than some signs and symptoms of anemia, and all of them were resolved completely just by giving a few-day break for the hydroxyurea therapy and starting with smaller doses again.

Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) used to reduce inflammation and acute thromboembolic events. Although aspirin has similar anti-inflammatory effects with the other NSAIDs, it also suppresses the normal functions of PLTs, irreversibly. This property causes aspirin being different from other NSAIDs, which are reversible inhibitors. Aspirin acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the cyclooxygenase (COX) enzyme. Aspirin's ability to suppress the production of prostaglandins (PGs) and thromboxanes (TXs) is due to its irreversible inactivation of the COX enzyme required for PGs and TXs synthesis. PGs are the locally produced hormones with some diverse effects, including the transmission of pain into the brain and modulation of the hypothalamic thermostat and inflammation. TXs are responsible for the aggregation of PLTs to form blood clots. In another definition, low-dose aspirin use irreversibly blocks the formation of TXA2 in the PLTs, producing an inhibitory effect on the PLT aggregation during whole lifespan of the affected PLTs (8-9 days). Since PLTs do not have nucleus and DNA, they are unable to synthesize new COX enzyme once aspirin inhibited the enzyme. The antithrombotic

property of aspirin is useful to reduce the incidences of myocardial infarction, transient ischemic attack, and stroke (35). Heart attacks are caused primarily by blood clots, and low dose of aspirin is seen as an effective medical intervention to prevent a second myocardial infarction (36). According to the medical literature, aspirin may also be effective in prevention of colorectal cancers (37). On the other hand, aspirin has some side effects including gastric ulcers, gastric bleeding, worsening of asthma, and Reye syndrome in childhood and adolescence. Reye syndrome is a rapidly worsening brain disease (38). The first detailed description of Reye syndrome was in 1963 by an Australian pathologist, Douglas Reye (39). The syndrome mostly affects children, but it can only affect fewer than one in a million children a year (39). It usually starts just after recovery from a viral infection, such as influenza or chicken pox (39). Symptoms of Reye syndrome may include personality changes, confusion, seizures, and loss of consciousness (38). Although the liver toxicity typically occurs in the syndrome and the liver is enlarged in most cases, jaundice is usually not seen with it (38). Early diagnosis improves outcomes, and treatment is supportive. Mannitol may be used in cases with the brain swelling (39). Although the death occurs in 20-40% of patients, about one third of survivors get a significant degree of brain damage (38). Interestingly, about 90% of cases in children are associated with an aspirin use (40). Due to the risk of Reye syndrome, the US Food and Drug Administration recommends that aspirin or aspirin-containing products should not be prescribed for febrile patients under the age of 16 years (41). Eventually, the general recommendation to use aspirin in children has been withdrawn, and it was only recommended for Kawasaki disease (38). When aspirin use was withdrawn for children in the US and UK in the 1980s, a decrease of more than 90% of Reye syndrome was seen (39). Due to the higher side effects of corticosteroids in long term, and due to the very low risk of Reye syndrome but much higher risk of death due to the SCDs even in children, aspirin should be added into the acute and chronic phase treatments of the SCDs with an anti-inflammatory dose even in childhood (42).

ACS is a significant cause of mortality in the SCDs (43). It occurs most often as a single episode, and a past history is associated with a higher mortality rate (43). Similarly, all of 14 patients with ACS had just a single episode, and two of them were fatal in spite of the immediate RBCs and ventilation supports and antibiotic therapy in the present study. The remaining 12 patients are still alive without a recurrence at the end of the 10-year follow up period. ACS is the most common between two to four years of age, and its incidence decreases with aging (44). As a difference from atherosclerotic consequences, the incidence of ACS did not show an increase with aging in the present study, and the mean ages of the patients with ACS and SCDs were similar (30.3 vs 30.5 years, $p>0.05$, respectively). The decreased incidence with aging may be due to the high mortality rate during the first episode and/or an acquired immunity against various antigens, and/or decreased strength of immune response by aging. Probably, ACS shows an inborn severity of the SCDs, and the incidence of ACS is higher in severe patients such as patients with the SCA and higher WBCs counts (43, 44). According to our long term experiences on the SCDs, the increased metabolic rate during infections accelerates sickling, thrombocytosis, leukocytosis, and capillary endothelial damage and edema, and terminates with end-organ failures-induced sudden deaths. ACS may also be a collapse of the pulmonary vasculature during such infections, and the exaggerated immune response against the sickled or just hardened RBCs-induced diffuse capillary endothelial damage may be important in the high mortality rate. A preliminary result from the Multi-Institutional Study of Hydroxyurea in the SCDs indicating a significant reduction of episodes of ACS with hydroxyurea therapy suggests that a considerable number of episodes are exaggerated with the increased numbers of WBCs and PLTs (45). Similarly, we strongly recommend hydroxyurea for all patients that may also be the cause of low incidence of ACS in our follow up cases (2.7% in males and 3.7% in females). Additionally, ACS did not show an infectious etiology in 66% (43, 44), and 12 of 27 cases with ACS had evidence of fat embolism in the other study (46). Beside that some authors indicated that antibiotics did not shorten the clinical course (47). RBCs support must be given as earliest as possible. RBCs support has the obvious benefits of decreasing sickle cell concentration directly, and suppressing bone marrow for the production of abnormal RBCs and excessive WBCs and PLTs. So they prevent further sickling-induced exaggerated capillary endothelial edema, disseminated tissue hypoxia, and end-organ failures-induced sudden deaths in the SCDs.

PHT is a condition of increased BPs within the arteries of the lungs. Shortness of breath, fatigue, chest pain, palpitation, swelling of legs and ankles, and cyanosis are common symptoms of PHT. Actually, it is not a diagnosis itself, instead solely a hemodynamic state characterized by resting mean pulmonary artery pressure of 25 mmHg or higher. An increase in pulmonary artery systolic pressure, estimated noninvasively by the echocardiography, helps to identify patients with PHT (48). The cause is often unknown. The underlying mechanism typically involves inflammation, fibrosis, and subsequent remodelling of the arteries. According to World Health Organization, there are five groups of PHT including pulmonary arterial hypertension, PHT secondary to left heart diseases, PHT secondary to lung diseases, chronic thromboembolic PHT, and PHT with unknown mechanisms (49). PHT affects about 1% of the world population, and its prevalence may reach 10% above the age of 65 years (50). Onset is typically seen between 20 and 60 years of age (49). The most common causes are CHD and COPD (49, 51). The cause of PHT in COPD is generally assumed to be hypoxic pulmonary vasoconstriction leading to permanent medial hypertrophy (52). But the pulmonary vascular remodeling in the COPD may have a much more complex mechanism than just being the medial hypertrophy secondary to the long-lasting hypoxic vasoconstriction alone (52). In fact, all layers of the vessel wall appear to be involved with prominent intimal changes (52). The specific pathological

picture could be explained by the combined effects of hypoxia, prolonged stretching of hyperinflated lungs-induced mechanical stress and inflammatory reaction, and the toxic effects of cigarette smoke (52). On the other hand, PHT is also a common consequence, and its prevalence was detected between 20% and 40% in the SCDs (53, 54). Whereas we detected the ratio as 12.2% in the present study. The relatively younger mean ages of the study cases (30.8 years of males and 30.3 years of females) may be the cause of the lower prevalence of PHT in the present study. Although the higher prevalences of smoking and alcohol-like atherosclerotic risk factors in male gender, and although the higher prevalences of disseminated teeth losses, ileus, cirrhosis, leg ulcers, digital clubbing, CRD, COPD, and stroke-like atherosclerotic consequences in male gender, and the male gender alone is being a risk factor for the systemic atherosclerosis, the similar prevalences of PHT and ACS in both genders also support nonatherosclerotic backgrounds of them in the SCDs in the present study. Similar to our result, women have up to four times of the risk of men for development of idiopathic PHT, and generally develop symptoms 10 years earlier than men in the literature with the unknown reasons, yet (55). Although COPD and CHD are the most common causes of PHT in the society (51, 56), and although COPD (25.2% vs 7.0%, $p<0.001$) and CHD (18.0% vs 13.2%, $p<0.05$) were higher in male gender in the present study, PHT was not higher in males, again. In another definition, PHT may have a sickled or just hardened RBCs-induced chronic thromboembolic whereas ACS may have an acute thromboembolic backgrounds in the SCDs (57, 58), because the mean age of ACS was lower than PHT (30.3 and 34.0 years, $p<0.05$), but its mortality was much higher than PHT in the literature (43, 44, 49).

COPD is the third leading cause of death with various underlying etiologies all over the world (59, 60). Aging, physical inactivity, sedentary lifestyle, animal-rich diet, smoking, alcohol, male gender, excess weight, chronic inflammations, prolonged infections, and cancers may be the major underlying causes. Beside smoking, regular alcohol consumption is also an important risk factor for the pulmonary and systemic atherosclerotic processes, since COPD was one of the most common diagnoses in alcohol dependence (61). Furthermore, 30-day readmission rates were higher in the COPD patients with alcoholism (62). Probably an accelerated atherosclerotic process is the main structural background of functional changes seen with the COPD. The inflammatory process of vascular endothelium is enhanced by release of various chemicals by inflammatory cells, and it terminates with an advanced fibrosis, atherosclerosis, and pulmonary losses. COPD may just be the pulmonary consequence of the systemic atherosclerotic process. Since beside the accelerated atherosclerotic process of the pulmonary vasculature, there are several reports about coexistence of associated endothelial inflammation all over the body in COPD (63, 64). For example, there may be close relationships between COPD, CHD, PAD, and stroke (65), and CHD was the most common cause of deaths in the COPD in a multi-center study of 5.887 smokers (66). When the hospitalizations were researched, the most common causes were the cardiovascular diseases, again (66). In another study, 27% of mortality cases were due to the cardiovascular diseases in the moderate and severe COPD (67). Similarly, COPD may just be the pulmonary consequence of the systemic atherosclerotic process caused by the sickled or just hardened RBCs in the SCDs (59).

Digital clubbing is characterized by the increased normal angle of 165° between nailbed and fold, increased convexity of the nail fold, and thickening of the whole distal finger (68). Although the exact cause and significance is unknown, the chronic tissue hypoxia is highly suspected (69). In the previous study, only 40% of clubbing cases turned out to have significant underlying diseases while 60% remained well over the subsequent years (18).

But according to our experiences, digital clubbing is frequently associated with the pulmonary, cardiac, renal, or hepatic diseases or smoking which are characterized by chronic tissue hypoxia (5). As an explanation for that hypothesis, lungs, heart, kidneys, and liver are closely related organs which affect each other's functions in a short period of time. Similarly, digital clubbing is also common in the SCDs, and its prevalence was 10.8% in the present study. It probably shows chronic tissue hypoxia caused by disseminated endothelial damage, inflammation, edema, and fibrosis at the capillaries in the SCDs. Beside the effects of SCDs, smoking, alcohol, cirrhosis, CRD, CHD, and COPD, the higher prevalence of digital clubbing in males (14.8% vs 6.6%, $p<0.001$) may also show some additional risks of male gender in the systemic atherosclerosis.

Leg ulcers are seen in 10% to 20% of the SCDs, and the ratio was 13.5% in the present study (70). Its prevalence increases with aging, male gender, and SCA (71). Similarly, its ratio was higher in males (19.8% vs 7.0%, $p<0.001$), and mean age of the leg ulcer patients was higher than the remaining ones in the present study (35.3 vs 29.8 years, $p<0.000$). The leg ulcers have an intractable nature, and around 97% of them relapse in a period of one year (70). As an evidence of their atherosclerotic background, the leg ulcers occur in the distal segments of the body with a lesser collateral blood supply (70). The sickled or just hardened RBCs-induced chronic endothelial damage, inflammation, edema, and fibrosis at the capillaries may be the major causes, again (71). Prolonged exposure to the sickled or just hardened bodies due to the pooling of blood in the lower extremities may also explain the leg but not arm ulcers in the SCDs. The sickled or just hardened RBCs-induced venous insufficiencies may also accelerate the highly destructive process by pooling of causative bodies in the legs, and vice versa. Pooling of blood may also have some effects on development of venous ulcers, diabetic ulcers, Buerger's disease, digital clubbing, and onychomycosis in the lower extremities. Furthermore, pooling of blood may be the main cause of delayed wound and fracture healings in the lower extremities. Smoking and alcohol may also have some additional

atherosclerotic effects on the leg ulcers in males. Although presence of a continuous damage of hardened RBCs on vascular endothelium, severity of the destructive process is probably exaggerated by the patients' own immune systems. Similarly, lower WBCs counts were associated with lower crises rates, and if a tissue infarct occurs, lower WBCs counts may decrease severity of pain and tissue damage (31). Because the main action of hydroxyurea may be the suppression of hyperproliferative WBCs and PLTs in the SCDs (72), prolonged resolution of leg ulcers with hydroxyurea may also suggest that the ulcers may be secondary to increased WBCs and PLTs counts-induced exaggerated capillary endothelial inflammation and edema.

Cirrhosis was the 10th leading cause of death for men and the 12th for women in the United States (6). Although the improvements of health services worldwide, the increased morbidity and mortality of cirrhosis may be explained by prolonged survival of the human being, and increased prevalence of excess weight all over the world. For example, nonalcoholic fatty liver disease (NAFLD) affects up to one third of the world population, and it became the most common cause of chronic liver disease even at childhood, nowadays (73). NAFLD is a marker of pathological fat deposition combined with a low-grade inflammation which results with hypercoagulability, endothelial dysfunction, and an accelerated atherosclerosis (73). Beside terminating with cirrhosis, NAFLD is associated with higher overall mortality rates as well as increased prevalences of cardiovascular diseases (74). Authors reported independent associations between NAFLD and impaired flow-mediated vasodilation and increased mean carotid artery intima-media thickness (CIMT) (75). NAFLD may be considered as one of the hepatic consequences of the metabolic syndrome and SCDs (76). Probably smoking also takes role in the inflammatory process of the capillary endothelium in liver, since the systemic inflammatory effects of smoking on endothelial cells is well-known with Buerger's disease and COPD (77). Increased oxidative stresses, inactivation of antiproteases, and release of proinflammatory mediators may terminate with the systemic atherosclerosis in smokers. The atherosclerotic effects of alcohol is much more prominent in hepatic endothelium probably due to the highest concentrations of its metabolites there. Chronic infectious or inflammatory processes and cancers may also terminate with an accelerated atherosclerosis in whole body (78). For example, chronic hepatitis C virus (HCV) infection raised CIMT, and normalization of hepatic function with HCV clearance may be secondary to reversal of favourable lipids observed with the chronic infection (78, 79). As a result, cirrhosis may also be another atherosclerotic consequence of the SCDs.

The increased frequency of CRD can also be explained by aging of the human being, and increased prevalence of excess weight all over the world (80, 81). Aging, physical inactivity, sedentary lifestyle, animal-rich diet, excess weight, smoking, alcohol, inflammatory or infectious processes, and cancers may be the main underlying causes of the renal endothelial inflammation. The inflammatory process is enhanced by release of various chemicals by lymphocytes to repair the damaged endothelial cells of the renal arteriols. Due to the continuous irritation of the vascular endothelial cells, prominent changes develop in the architecture of the renal tissues with advanced atherosclerosis, tissue hypoxia, and infarcts. Excess weight-induced hyperglycemia, dyslipidemia, elevated BPs, and insulin resistance may cause tissue inflammation and immune cell activation (82). For example, age ($p= 0.04$), high-sensitivity C-reactive protein ($p= 0.01$), mean arterial BPs ($p= 0.003$), and DM ($p= 0.02$) had significant correlations with the CIMT (81). Increased renal tubular sodium reabsorption, impaired pressure natriuresis, volume expansion due to the activations of sympathetic nervous system and renin-angiotensin system, and physical compression of kidneys by visceral fat tissue may be some mechanisms of the increased BPs with excess weight (83). Excess weight also causes renal vasodilation and glomerular hyperfiltration which initially serve as compensatory mechanisms to maintain sodium balance due to the increased tubular reabsorption (83). However, along with the increased BPs, these changes cause a hemodynamic burden on the kidneys in long term that causes chronic endothelial damage (84). With prolonged weight excess, there are increased urinary protein excretion, loss of nephron function, and exacerbated HT. With the development of dyslipidemia and DM in cases with excess weight, CRD progresses much faster (83). On the other hand, the systemic inflammatory effects of smoking on endothelial cells may also be important in the CRD (85). Although some authors reported that alcohol was not related with the CRD (85), various metabolites of alcohol circulate even in the renal capillaries, and give harm to the renal capillary endothelium. Chronic inflammatory or infectious processes may also terminate with the accelerated atherosclerosis in the renal vasculature (78). Although CRD is due to the atherosclerotic process of the renal vasculature, there are close relationships between CRD and other atherosclerotic consequences of the metabolic syndrome including CHD, COPD, PAD, cirrhosis, and stroke (86), and the most common cause of death was the cardiovascular diseases in the CRD again (87). The sickled or just hardened RBCs-induced capillary endothelial damage may be the main cause of CRD in the SCDs, again (88).

Stroke is an important cause of death, and usually develops as an acute thromboembolic event on the chronic atherosclerotic background. Aging, male gender, smoking, alcohol, and excess weight may be the major underlying causes. Stroke is a common complication of the SCDs, too (89, 90). Similar to the leg ulcers, stroke is particularly higher with the SCA and higher WBCs counts (91). Sickling-induced capillary endothelial damage, activations of WBCs, PLTs, and coagulation system, and hemolysis may cause inborn and severe capillary endothelial inflammation, edema, and fibrosis (92). Probably, stroke may not have a macrovascular origin in the SCDs, and diffuse capillary endothelial inflammation, edema, and fibrosis may be much more important. Infections, inflammations, medical

or surgical emergencies, and emotional stresses may precipitate stroke by increasing basal metabolic rate and sickling. A significant reduction of stroke with hydroxyurea may also suggest that a significant proportion of cases is developed secondary to the increased WBCs and PLTs-induced exaggerated capillary endothelial inflammation and edema (45).

The venous capillary endothelium may also be involved in the SCDs (93). Normally, leg muscles pump veins against the gravity, and the veins have pairs of leaflets of valves to prevent blood from flowing backwards. When the leaflets are damaged, varices and telangiectasias develop. DVT may also cause varicose veins and telangiectasias. Varicose veins are the most common in superficial veins of the legs, which are subject to higher pressure when standing up, thus physical examination must be performed in the upright position. Although the relatively younger mean ages and significantly lower body mass index of the SCDs cases in the literature (10), the prevalences of DVT and/or varices and/or telangiectasias of the lower limbs were relatively higher in the present study (9.0% vs 6.6% in males and females, $p>0.05$, respectively), indicating an additional venous involvement of the SCDs. Similarly, priapism is the painful erection of penis that cannot return to its flaccid state within four hours in the absence of any stimulation (94). It is an emergency because repeated damaging of the blood vessels may terminate with fibrosis of the corpus cavernosa, a consecutive erectile dysfunction, and eventually a shortened, indurated, and non-erectile penis (94). It is mainly seen with SCDs, spinal cord lesions (hanging victims), and glucose-6-phosphate dehydrogenase deficiency (95, 96). Ischemic (veno-occlusive), stuttering (recurrent ischemic), and nonischemic priapisms (arterial) are the three types (97). Ninety-five percent of clinically presented priapisms are the ischemic (veno-occlusive) disorders in which blood cannot return adequately from the penis as in the SCDs, and they are very painful (94, 97). RBCs support is the treatment of choice in acute whereas hydroxyurea should be the treatment of choice in chronic phases (98). According to our experiences, hydroxyurea is highly effective for prevention of attacks and consequences of priapism if iniatiated in early years of life, but it may be difficult due to the excessive fibrosis around the capillaries if initiated later in life.

As a conclusion, the sickled or just hardened RBCs-induced capillary endothelial damage, inflammation, edema, and fibrosis are initiated at birth, and terminate with disseminated tissue hypoxia, multiorgan failures, and sudden deaths even at childhood. Although RBCs suspensions and corticosteroids in acute and aspirin plus hydroxyurea in acute and chronic phases decrease severity of the inflammatory process, survivals are still shortened in both genders, dramatically. Infections, medical or surgical emergencies, or emotional stresses-induced increased basal metabolic rate aggravates the sickling and capillary endothelial edema, and may terminate with multiorgan failures-induced sudden deaths in the SCDs.

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Fasting plasma glucose may behave as a positive in mild but as a negative acute phase reactant in moderate and severe inflammatory disorders

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Abstract

Background: There may be significant relationships between fasting plasma glucose (FPG) and severity of inflammations.

Method: All cases with digital clubbing were included.

Results: The study included 104 cases with clubbing detected among 2.428 cases (1.044 males). So clubbing was higher in males (8.1% versus 1.3%, p<0.001). Mean age of clubbing cases was 49.2 years, and there was a male predominance (81.7%), again. Parallel to the male predominance, there were higher prevalences of smoking (69.2% versus 41.6%, p<0.001), chronic obstructive pulmonary disease (COPD) (27.8% versus 10.8%, p<0.001), and coronary heart disease (CHD) and/or peripheric artery disease (PAD) (7.6% versus 0.0%, p<0.01) in the clubbing cases. Whereas the body weight, body mass index (BMI), and FPG were lower in the clubbing cases but the differences were nonsignificant probably due to the small sample size. But diabetes mellitus (DM) (12.5% versus 21.6%, p<0.05) and systolic blood pressure (BP) (127.6 versus 136.9 mmHg, p= 0.011) were lower in the clubbing cases, significantly.

Conclusion: There are significant relationships between smoking, digital clubbing, COPD, CHD, and PAD probably due to strong atherosclerotic effects of smoking. Similarly, the body weight, BMI, FPG, systolic BP, and DM are inversely related with the clubbing probably due to the severe inflammatory effects of smoking on the vascular endothelium, again. FPG may behave as a positive acute phase reactant (APR) in mild inflammatory disorders such as irritable bowel syndrome but as a negative APR in moderate and severe inflammatory disorders such as smoking, digital clubbing, and sickle cell diseases.

Key words: Fasting plasma glucose, diabetes mellitus, irritable bowel syndrome, smoking, digital clubbing, sickle cell diseases, atherosclerosis

Introduction

Digital changes may help to identify some systemic disorders in human body. Digital clubbing is a deformity of the fingers and fingernails that is known for a long time. It is characterized by bulbous enlargement of the distal phalanges due to the increase in soft tissue. Digital clubbing develops in the following steps; fluctuation and softening of the nailbed, loss of normal angle between the nailbed and fold which is lower than 165°, increased convexity of the nail fold, thickening of the whole distal finger, and shiny aspect and striation of the nail and skin (1). Schamroth's window test is a popular test for the diagnosis of digital clubbing (2). When the distal phalanges of corresponding fingers of opposite hands are directly opposed, a small diamond-shaped 'window' is apparent between the nailbeds, normally. If this window is obliterated, the test is positive and digital clubbing is present. Although many disorders may be associated with the clubbing, the reports are mostly anecdotal, and prospective studies of patients with the clubbing have not been performed, yet. The clubbing may be associated with pulmonary, cardiac, and hepatic diseases that are featuring with chronic tissue hypoxia (tuberculosis, bronchiectasis), hypothyroidism, gastrointestinal and hepatobiliary disorders (malabsorption, Crohn's disease, ulcerative colitis, cirrhosis), thymoma, thalassemia, and human immunodeficiency virus infection (3-7). But there was not any underlying disorder in 60% of cases (8). Additionally, the exact prevalence of digital clubbing in the population is not known. The above study detected digital clubbing just in 0.9% of all patients admitted to the Department of Internal Medicine, and 66.6% of the clubbing cases were male (8). Probably due to the higher prevalence of smoking in males (9), the great gender differences were observed in the clubbing. We tried to understand whether or not there are some relationships between fasting plasma glucose (FPG) and severity of inflammations in human body.

Matertials and Methods

The study was performed in the Internal Medicine Clinic of the Mustafa Kemal University between March 2007 and May 2011 on all patients applying for any complaint. Their medical histories including smoking, claudication, angina pectoris, and already used medications were learnt, and a routine check up procedure including FPG, total cholesterol, high density lipoproteins (HDL), triglycerides, an electrocardiography, and a Doppler echocardiogram just in suspected cases was performed. Digital clubbing is diagnosed by determining ratio of the distal phalangeal diameter to the interphalangeal diameter which is required to be greater than 1.0, and with the presence of the Schamroth sign (2, 8). Current daily smokers at least for the last six months and cases with a history of five pack-years were accepted as smokers. Body mass index (BMI) of each case was calculated by the measurements of the Same Physician instead of verbal expressions (10). Office blood pressure (BP) was checked after a five-minute of rest in seated position with the mercury sphygmomanometer (ERKA, Germany). Cases with an overnight FPG level of 126 mg/dL or higher on two occasions or already using antidiabetic medications were defined as diabetics (10). An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 100 and 125 mg/dL, and diagnosis of cases with a two-hour plasma glucose level of 200 mg/dL or greater was diabetes mellitus (DM) (10). An exercise electrocardiogram was performed just in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography was taken just for exercise electrocardiogram positive cases. So coronary heart disease (CHD) was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders of the cardiac walls. A colored Doppler ultrasonograpy of arterial system of the lower extremities were obtained just in cases with a history of claudication for the diagnosis of peripheric artery disease (PAD). Chronic obstructive pulmonary disease (COPD) was diagnosed by means of spirometric measurements. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (11). Eventually, all cases with the clubbing were collected into the first, and age- and sex-matched control cases were collected into the second groups, and compared in between. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 104 patients (85 males) with the digital clubbing and 120 control cases. The clubbing cases were detected among 2.428 cases (1.044 males), totally. So clubbing was higher in males, significantly (8.1% versus 1.3%, $p<0.001$). The mean age of clubbing cases was 49.2 years, and there was a male predominance in them (81.7%), again. Parallel to the male predominance, there were higher prevalences of smoking (69.2% versus 41.6%, $p<0.001$), COPD (27.8% versus 10.8%, $p<0.001$), and CHD and/or PAD (7.6% versus 0.0%, $p<0.01$) in the clubbing cases. Whereas the body weight, BMI, and FPG were lower in the clubbing cases, but the differences were nonsignificant probably due to the small sample size. But DM (12.5% versus 21.6%, $p<0.05$) and systolic BP (127.6 versus 136.9 mmHg, $p= 0.011$) were lower in the clubbing cases, significantly. The mean pack-years were similar both in the clubbing and control groups (28.5 versus 28.0 years, respectively, $p>0.05$). On the other hand, low density lipoproteins (LDL) (130.0 versus 126.9 mg/dL, $p>0.05$) and triglycerides (152.5 versus 143.4 mg/dL, $p>0.05$) were higher in the digital clubbing cases but the differences were nonsignificant probably due to the small sample size of the study, again. There were seven cases with CHD and one case with PAD in the clubbing group, whereas no case could be detected in the control group (Table 1).

Table 1: Characteristic features of the study cases

Variables	Cases with clubbing	*p*-value	Control cases
Number	104		120
Age (year)	49.2 ± 15.2 (21-81)	Ns*	49.3 ± 16.2 (21-82)
Male ratio	***81.7% (85)***	Ns	81.6% (98)
Smoking	***69.2% (72)***	***<0.001***	41.6% (50)
COPD†	***27.8% (29)***	***<0.001***	10.8% (13)
BMI‡ (kg/m²)	26.4 ± 4.9 (16.1-40.5)	Ns	***27.3 ± 4.6 (17.1-39.2)***
Weight (kg)	74.3 ± 14.0 (38-120)	Ns	***77.9 ± 13.6 (45-116)***
FPG§ (mg/dL)	113.7 ± 43.5 (73-301)	Ns	***120.8 ± 40.8 (68-271)***
DM‖	12.5% (13)	***<0.05***	***21.6% (26)***
LDL¶ (mg/dL)	***130.0 ± 38.0 (10-237)***	Ns	126.9 ± 35.7 (54-265)
Triglycerides (mg/dL)	***152.5 ± 79.3 (55-438)***	Ns	143.4 ± 79.8 (49-383)
Systolic BP** (mmHg)	127.6 ± 25.6 (80-200)	***0.011***	***136.9 ± 28.0 (80-220)***
Diastolic BP (mmHg)	88.0 ± 12.5 (60-120)	Ns	88.3 ± 12.2 (50-120)
CHD and/or PAD****	***7.6% (8)***	***<0.01***	0.0% (0)

*Nonsignificant (p>0.05) †Chronic obstructive pulmonary disease ‡Body mass index §Fasting plasma glucose
‖Diabetes mellitus ¶Low density lipoproteins **Blood pressure ***Coronary heart disease
****Peripheric artery disease

Discussion

Recurrent upper abdominal discomfort may be the cause of nearly half of applications to the Internal Medicine Clinics (12), and irritable bowel syndrome (IBS) and chronic gastritis may be the most commonly diagnosed disorders in such cases. Flatulence, periods of diarrhea and constipation, repeated toilet visits due to urgent evacuation or early filling sensation, excessive straining, feeling of incomplete evacuation, frequency, urgency, reduced feeling of well-being, and eventually disturbed social life are often reported by the patients with IBS. Although many patients relate onset of symptoms to intake of food, and often incriminate specific food items, a meaningful dietary role is doubtful in the IBS. According to the literature, nearly 20% of general population have IBS, and it is more common in females with unknown causes, yet (13). Psychological factors seem to precede onset and exacerbation of gut symptoms, and many potentially psychiatric disorders including anxiety, depression, sleep disorders, illness fear, cancer fear, or death fear usually coexist with the IBS (14). For example, thresholds for sensations of initial filling, evacuation, urgent evacuation, and utmost tolerance recorded via a rectal balloon significantly decreased by focusing the examiners' attention on gastrointestinal stimuli by reading pictures of gastrointestinal malignancies in patients with the IBS (15). In other words, although IBS is described as a physical disorder according to Rome II guidelines, psychological factors may be crucial for triggering of these physical changes in the body. Eventually, IBS may even terminate with chronic gastritis, urolithiasis, and hemorrhoids (16-18). Similarly, some authors studied the role of inflammation in IBS via colonic biopsies in 77 patients (19). Although 38 patients had normal histology, 31 patients demonstrated microscopic inflammation, and eight patients fulfilled criteria for lymphocytic colitis. However, immunohistology revealed increased intraepithelial lymphocytes as well as increased CD3 and CD25 positive cells in lamina propria of the group with "normal" histology. These features were more evident in the microscopic inflammation group who additionally revealed increased neutrophils, mast cells, and natural killer cells. All of these immunopathological abnormalities were the most evident in the lymphocytic colitis group who also demonstrated HLA-DR staining in the crypts and increased CD8 positive cells in the lamina propria (19). A direct link between the immunologic activation and IBS symptoms was shown by some other authors, too (20). They demonstrated not only an increased mast cell degranulation in the colon but also a direct correlation between proximity of mast cells to neuronal elements and severity of pain in the IBS (20). In addition to above findings, there are some evidences for extension of the inflammatory process behind the mucosa. Some authors addressed this issue in ten patients with severe IBS by examining full-thickness jejunal biopsies obtained via laparoscopy (21). They detected a low-grade infiltration of lymphocytes in myenteric plexus of nine patients, four of whom had an associated increase in intraepithelial lymphocytes and six demonstrated evidence of neuronal degeneration (21). Nine patients had hypertrophy of longitudinal muscles, and seven had abnormalities in number and size of interstitial cells of Cajal (21). The finding of intraepithelial lymphocytosis was also consistent with some other reports in the colon (19) and duodenum (22). So IBS may have more complex mechanisms affecting various systems of the body by means of a low-grade inflammatory process (23). Beside that mean values of FPG (111.9 versus 105.4 mg/dL, p= 0.002) and plasma triglycerides (167.0 versus 147.3 mg/dL, p= 0.013) were higher in the IBS cases (24). Because plasma triglycerides are well-known acute phase reactants (APRs), the additionally increased FPG in the IBS cases may show the fact that FPG may behave as a positive APR in the IBS cases (24).

Sickle cell diseases (SCDs) are chronic inflammatory process on vascular endothelium, initiated at birth and terminated with an accelerated atherosclerosis induced end-organ failures in early years of life (25, 26). Hemoglobin S causes loss of elastic and biconcave disc shaped structures of red blood cells (RBCs). Probably loss of elasticity is the main problem instead of the shape since sickling is rare in peripheric blood samples of the patients with associated thalassemia minors, and human survival is not affected in hereditary spherocytosis or elliptocytosis. Loss of elasticity is present during whole lifespan, but exaggerated with inflammation, infection, depression, and various stresses of the body. The hardened RBCs induced chronic endothelial damage, inflammation, and fibrosis terminate with disseminated tissue hypoxia all over the body (27). As a difference from other causes of chronic endothelial damage, the SCDs may keep vascular endothelium particularly at the capillary level (28, 29), since the capillary system is the main distributor of the hardened RBCs into the tissues. The hardened RBCs induced chronic endothelial damage builds up an advanced atherosclerosis in early years of life. Vascular narrowings and occlusions induced tissue ischemia and infarctions are the final consequences, so the mean life expectancy is decreased by 25 to 30 years in both genders in the SCDs (26). Due to the severity of inflammation in the SCDs, the body weight, BMI, FPG, LDL, HDL, systolic and diastolic BPs, and hematocrit values decreased as some negative APRs in the body, significantly (30).

The monolayer of endothelial cells that forms the inner lining of arteries, veins, capillaries, and lymphatics is called as the endothelium. Probably, the whole endothelium all over the body may act as a private organ that may be the largest organ of the body. It may contract vasculature of the peripheral organs while relaxing the internal ones during cold, anxiety, and depression-like stresses. Because we measure the systolic and diastolic BPs of the arms and legs, they may not show the actual BPs of the brain, heart, lung, liver, and kidney-like internal organs. The endothelium may be the main organ in the control of blood fluidity, platelets aggregation, and vascular tone in the body. It may control vascular tone and blood flow by releasing nitric oxide, reactive oxygen species, and metabolites of arachidonic acid into the circulation. It may also be important for synthesizing of vasoactive hormones

such as angiotensin II. An endothelial dysfunction-induced accelerated atherosclerosis all over the body may be the main cause of end-organ insufficiencies, aging, and death. Such a dysfunction may also be important in the development of cancers by preventing clearance of malignant cells by the natural killers in terminal points of the circulation. Similarly, physical inactivity, animal-rich diet, excess weight, higher BP and glucose levels, chronic inflammations, prolonged infections, cancers, smoking, and alcohol may be accelerating factors of the chronic endothelial inflammation and dysfunction terminating with the accelerated atherosclerosis-induced end-organ insufficiencies (31). The much higher BPs of the afferent vasculature may be the major accelerating factor by inducing recurrent injuries on the vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Due to the chronic endothelial damage, inflammation, edema, fibrosis, and dysfunction, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood flow to the terminal organs, and increase systolic and decrease diastolic BPs further. Some of the irreversible consequences of the systemic inflammatory process are obesity, hypertension (HT), DM, cirrhosis, PAD, COPD, CHD, chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, dementia, aging, and death (32). Although early withdrawal of the accelerating factors may delay terminal consequences, endothelial changes cannot be reversed, completely after development of the irreversible end-points due to their fibrotic natures. The accelerating factors and irreversible end-points are researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome, extensively (33, 34).

Obesity may be one of the irreversible end-points of the metabolic syndrome. Although some transient successes can be achieved, nonpharmaceutical approaches provide limited benefit to reverse the obesity, permanently. Due to the excess weight-induced chronic low-grade inflammation on the vascular endothelium, the risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess weight in all age groups (35). The chronic low-grade inflammation may even cause genetic changes of the endothelial cells, and the systemic atherosclerosis may prevent clearance of malignant cells, effectively. Similarly, the effects of excess weight on the BP were shown in the literature, extensively (36). For example, prevalences of sustained normotension (NT) were higher in the underweight than the normal weight (80.3% versus 64.0%, $p<0.05$) and overweight groups (80.3% versus 31.5%, $p<0.001$) (36), and 52.8% of patients with HT had obesity against 14.5% of patients with the sustained NT ($p<0.001$) (37). So the major underlying cause of the metabolic syndrome appears as weight gain that may be the main cause of insulin resistance, impaired fasting glucose, impaired glucose tolerance, hyperlipoproteinemias, and white coat hypertension (WCH) (38). Interestingly, weight gain before the development of an obvious overweight or obesity may even cause development of several components of the syndrome. For example, WCH alone may be a strong indicator of weight gain even before development of excess weight (36, 37). On the other hand, prevention of the weight gain with physical activity even in the absence of a prominent weight loss usually results with resolution of many parameters of the syndrome (39). According to our experiences, excess weight may actually be a result of physical inactivity instead of an excessive eating habit. In another word, there is a problem with burning of calories instead of getting them. Thus prevention of weight gain cannot be achieved by diet, alone (40). On the other hand, limitation of excess weight as an excessive fat tissue around abdomen under the heading of abdominal obesity may be meaningless, instead it should be defined as overweight or obesity by means of the BMI. Because adipocytes function as an endocrine organ, and they release leptin, tumour necrosis factor (TNF)-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines into the plasma (41). Eventual hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with insulin resistance, elevated BPs, and chronic endothelial inflammation and dysfunction. Similarly, the Adult Treatment Panel (ATP) III reported that although some people classified just as overweight with larger muscular masses, most of them also have excess fat tissue predisposing to the irreversible end-points of the metabolic syndrome (10).

Smoking may be the second common cause of disseminated vasculitis in human body. It may cause a low-grade systemic inflammation on vascular endothelium terminating with an accelerated atherosclerosis-induced end-organ insufficiencies all over the body (42). Its atherosclerotic effect is the most obvious in Buerger's disease. Buerger's disease is an obliterative vasculitis characterized by inflammatory changes in the small and medium-sized arteries and veins, and it has never been reported in the absence of smoking. Plasma triglycerides, LDL, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) may be positive whereas HDL and FPG may be negative APRs indicating such inflammatory effects of smoking in the body (43). Parallel to the systemic inflammatory and atherosclerotic effects of smoking, smoking in human being and nicotine administration in animals were associated with the lower values of BMI in some studies (44). Some evidences revealed an increased energy expenditure during smoking both on the rest and light physical activity (45). Nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (46). According to an animal study, nicotine may lengthen intermeal time, and decrease amount of meal eaten (47). Smoking may be associated with a postcessation weight gain, but the risk is the highest during the first year, and decreases with the following years (48). As the opposite findings to the above studies, the mean weight and BMI were similar both in the smokers and non-smokers in the other study (43). Similarly, prevalences of smoking were similar in the normal weight (35.9%), overweight (32.9%), and obesity groups (33.7%, $p>0.05$ between all) in another study (49). On the

other hand, although the CHD was detected with similar prevalences in both genders, prevalences of smoking and COPD were higher in males against the higher BMI, LDL, triglycerides, WCH, HT, and DM in females (50). Beside that the prevalence of myocardial infarctions is increased three-fold in men and six-fold in women who smoked at least 20 cigarettes per day (51). In another word, smoking may be more dangerous for women about the atherosclerotic end-points probably due to the higher BMI and its consequences in them. Several toxic substances found in the cigarette smoke get into the circulation, and cause the vascular endothelial inflammation in various organ systems of the body. For example, smoking is usually reported together with depression, IBS, chronic gastritis, hemorrhoids, and urolithiasis in the literature (16, 52). There may be several underlying mechanisms to explain these associations in the smokers (52). First of all, smoking may have some additional antidepressant properties with several side effects. Secondly, smoking-induced vascular endothelial inflammation may disturb epithelial functions for absorption and excretion in the gastrointestinal and genitourinary tracts. These functional problems may terminate with urolithiasis and components of the IBS including loose stool, diarrhea, and constipation. Thirdly, diarrheal losses-induced urinary changes may even cause urolithiasis (16, 17). Fourthly, smoking-induced sympathetic nervous system activation may cause motility problems in the gastrointestinal and genitourinary tracts terminating with the IBS and urolithiasis. Eventually, immunosuppression secondary to smoking-induced vascular endothelial inflammation may even terminate with the gastrointestinal and genitourinary tract infections causing loose stool, diarrhea, and urolithiasis, because some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits in the urine. Actually, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infections with the bacteria producing urease. Parallel to the results above, urolithiasis was detected in 17.9% of cases with the IBS and 11.6% of cases without in the other study ($p<0.01$) (16).

Alcohol may be the third common cause of systemic vasculitis in human body. It is addictive to humans, and can result in alcohol use disorder (AUD), dependence, and withdrawal. Alcohol is causally associated with more than 200 different pathologies including cancers in whole body (53). Eventually, people hospitalized with AUD have an average life expectancy of 47-53 years in men and 50-58 years in women, and die 24-28 years earlier than the others (54). People with AUD have three-fold higher mortality in men and four-fold in women (55). Similar to smoking, alcohol may be more dangerous for women about the atherosclerotic end-points probably due to their lower body mass induced lower capacity to metabolize alcohol and higher body fat. A very substantial part of the Danish excess mortality and lower life expectancy compared to Sweden can be attributed to higher mortality related with alcohol and smoking (54). It may even cause unconsciousness and sudden death if taken in high amounts. Hepatic alcohol dehydrogenase is the main enzyme to metabolize alcohol that requires the cofactor, nicotinamide adenine dinucleotide (NAD). Normally, NAD is used to metabolize fats in the liver but alcohol competes with these fats for the use of NAD. Eventually, prolonged exposure of alcohol causes fatty liver. Ethanol is the only alcohol that is found in alcoholic beverages. Ethanol crosses biological membranes and blood-brain barrier by means of the passive diffusion, easily. Alcohol works particularly by increasing effects of the gamma aminobutyric acid that is the main inhibitory neurotransmitter of the brain. Alcohol causes happiness and euphoria, decreased anxiety, increased sociability, sedation, generalized depression of central nervous system, and impairment of cognitive, memory, motor, and sensory functions. It may even cause fetal disorders in pregnancy since ethanol is classified as a teratogen. Regular alcohol consumption leads to cell death in the liver, scarring, cirrhosis, and hepatocellular carcinoma. Heavy consumption may even terminate with permanent brain damage. Alcohol is the major contributing factor of elevated triglycerides which are the sensitive APRs in the plasma (38). Although regular alcohol consumers were excluded, plasma triglycerides were higher in the smokers (163.1 versus 151.3 mg/dL, $p<0.05$), indicating the inflammatory effects of smoking in the other study (56).

The acute phase response occurs in case of infection, infarction, cancer, trauma, depression, and burn-like inflammatory conditions of the body. Certain mediators known as APRs are increased or decreased during the response (57, 58). These markers are commonly used in the clinical practice as the indicators of acute and chronic inflammations in the body. The terms of acute phase proteins and APRs are usually used synonymously, although some APRs are polypeptides rather than proteins.

Positive and negative APRs are those whose concentrations increase or decrease during the acute phase response, respectively. The response is predominantly mediated by the pro-inflammatory cytokines including TNF, interleukin-1, and interleukin-6 secreted by neutrophils and macrophages into the circulation. The liver and other organs respond to the cytokines by producing many positive APRs. ESR, CRP, fibrinogen, ferritin, procalcitonin, hepcidin, haptoglobin, ceruloplasmin, complement proteins, and serum amyloid A are some of the well-known positive APRs. CRP is a useful indicator of the acute phase response, clinically. It is responsible for activation of the complement pathway. CRP reaches up to the maximum concentration within two days, and decreases with the resolution of the inflammation with a half-life of 6-8 hours, rapidly. It correlates with ESR, but not simultaneously since ESR is largely dependent upon elevation of fibrinogen with a half-life of one week, approximately. Thus ESR remains higher for a longer period of time despite the removal of the inflammatory stimulus. Similarly, white blood cells and platelet counts may also behave as some other positive APRs in the body (59). On the other hand, productions of the negative APRs are suppressed, simultaneously. Albumin, transferrin,

retinol-binding protein, antithrombin, transcortin, alpha-fetoprotein, and hemoglobin are some of the well-known negative APRs in the body. Suppressions of such negative APRs are also used as the indicators of the acute phase response in the body. Suppressions of such negative APRs may actually be secondary to the protection of amino acids and polypeptides required for the production of positive APRs, sufficiently. As also observed in the smokers in the above study (56), production of HDL may also be suppressed in the liver during the acute phase response (60). Similarly, triglycerides, DM, and CHD were all higher in patients with plasma HDL values of lower than 40 mg/dL, significantly (60). So HDL may actually behave as negative whereas triglycerides positive APRs in the plasma. Similarly, the highest CHD of the group with HDL values of lower than 40 mg/dL can also be explained by the same hypothesis in the other study (38). Additionally, plasma triglycerides increased whereas HDL decreased during infections (61). On the other hand, a 10 mg/dL increase of plasma LDL values was associated with a 3% lower risk of hemorrhagic stroke (62). Similarly, the highest prevalences of HT and DM parallel to the elevated values of LDL and HDL, and the highest prevalences of COPD, CHD, and CRD in contrast to the lowest values of LDL and HDL may show initially positive but eventually negative behaviors of LDL and HDL as the APRs (63). Probably, HDL turn to the negative direction much more earlier than LDL in the plasma. Interestingly, the most desired values were between 80 and 100 mg/dL for LDL, between 40 and 46 mg/dL for HDL, and lower than 60 mg/dL for triglycerides in the plasma (38). Parallel to ESR and CRP, plasma triglycerides and LDL may behave as positive whereas FPG and HDL negative APRs in smokers (56). In another word, lower HDL values should alert clinicians for researching of any acute phase response in the body (64, 65).

Cholesterol, triglycerides, and phospholipids are the major lipids of the body. They do not circulate in the plasma, freely instead they are bound to proteins, and transported as lipoproteins. There are five mjor classes of lipoproteins in the plasma. Chylomicrons carry exogenous triglycerides to the liver via the thorasic duct. Very low density lipoproteins (VLDL) are produced in the liver, and carry endogenous triglycerides to the organs. VLDL are converted into the intermediate density lipoproteins (IDL) by removal of 90% of triglycerides by lipases in the capillaries of adipocytes and muscle tissues. Then the IDL are degraded into LDL by removal of more triglycerides. So VLDL are the main source of LDL in the plasma, and LDL deliver cholesterol from the liver to organs. Although the liver removes majority of LDL from the circulation, a small amount is uptaken by scavenger receptors of the macrophages migrating into the arterial walls, and become the foam cells of atherosclerotic plaques. HDL remove fats and cholesterol from cells including the arterial wall atheroma, and carry the cholesterol back to the adrenals, ovaries, and testes-like steroidogenic organs and liver for excretion, re-utilization, or disposal. All of the carrier lipoproteins are under dynamic control, and are readily affected by diet, drugs, inflammations, infections, cancers, trauma, smoking, alcohol, and excess weight. Thus lipid analysis should be performed during a steady state. For example, the metabolic syndrome alone is a low grade inflammatory process, and it may even cause abnormal lipoproteins levels in the plasma. HDL may normally show various anti-oxidative, anti-inflammatory, and anti-atherogenic properties including reverse cholesterol transport (66). However, HDL may become 'dysfunctional' in pathologic conditions which means that relative compositions of lipids and proteins, as well as the enzymatic activities of HDL are altered (66). For example, properties of HDL are compromised in patients with DM by means of the oxidative modification, glycation, and/or transformation of HDL proteomes into the proinflammatory proteins. Additionally, the drugs increasing HDL values such as niacin, fibrates, and cholesteryl ester transfer protein inhibitors cannot reduce all cause mortality, CHD mortality, myocardial infarction, and stroke (67). In other words, HDL may just be some indicators instead of being the main actors of the health. Similarly, BMI, DM, and CHD were the lowest between the HDL values of 40 and 46 mg/dL, and the prevalence of DM was only 3.1% between these values against 22.2% outside these limits (68). Similar to the above study (56), HDL and FPG values were also suppressed in the SCDs, probably due to the severe inflammatory nature of the diseases (30). Smoking may reduce HDL and FPG by means of the inflammatory effects on the vascular endothelium all over the body (43). On the other hand, triglycerides may be the most sensitive APRs indicating the metabolic syndrome (69). Although ATP II determined the normal plasma triglycerides as lower than 200 mg/dL in 1994 (70), World Health Organisation in 1999 (71) and ATP III in 2001 reduced the normal limits as lower than 150 mg/dL (10). But there are still suspicions about the safest values of triglycerides in the plasma (69). Beside that triglycerides are the only lipids which were not suppressed with the pathological weight losses (72). For example, plasma triglycerides increased in contrast to the suppressed body weight and BMI in the SCDs (72). Similarly, prevalences of excess weight, DM, HT, and smoking were higher in the hypertriglyceridemia group (200 mg/dL and higher) in the other study (73). Interestingly, the greatest number of deteriorations in the metabolic parameters was observed with triglycerides values of 60 mg/dL and higher (69).

The body's homeostatic mechanism keeps blood glucose levels within a narrow range with two groups of mutually antagonistic hormones. Glucagon, cortisol, and catecholamines are the catabolic hormones increasing the blood glucose, whereas insulin is the anabolic hormone decreasing the blood glucose levels. Glucagon is secreted from the alpha cells while insulin is secreted from the beta cells of pancreatic islets which are the bundles of endocrine tissues. They regulate the blood glucose levels through a negative feedback mechanism together. When the blood glucose levels are too high, insulin tells muscles to take up excess glucose for storage. When the blood glucose levels are too low, glucagon informs the tissues to produce more glucose. Catecholamines prepare the muscles and respiratory system for a 'fight or

flight' response. Cortisol prepares the body for the various stresses. A blood glucose level of four grams, or about a teaspoon, is critical for the normal function of millions of cells in the body (74). The four grams of glucose circulate in the blood of a person with the weight of 70 kg. The constant blood glucose levels are maintained via the hepatic and muscular glycogen stores during fasting since glucose is stored in the skeletal muscles and hepatocytes in the form of glycogen. There are approximately 100 and 400 grams of glycogen stored in the skeletal muscles and liver, respectively (74). The brain consumes about 60% of the blood glucose during fasting. FPG is the most commonly used indication of overall glucose homeostasis, and it is measured after a fasting period of 8 hours. Infections, inflammations, surgical operations, depression, alcohol, and smoking-like stresses may affect the blood glucose homeostasis. For example, smoking was negatively associated with FPG and DM just in Chinese men with the normal weight, but not in men with excess weight or in women (75). Similarly, smokers have a lower likelihood of newly-diagnosed DM in Chinese men with a lower BMI in the other study (76). Parallel to the above studies, FPG and DM were also lower in smokers in the other study (102.3 versus 111.6 mg/dL, p=0.007 and 8.9% versus 14.3%, p<0.05, respectively), and although majority of the smokers were male again (70.0%), BMI of the smokers was higher (26.6 kg/m2) in contrast to the above studies (56).

As a conclusion, there are some significant relationships between the digital clubbing, smoking, COPD, CHD, and PAD probably due to strong atherosclerotic effects of smoking. Similarly, the mean weight, BMI, FPG, systolic BP, and DM are inversely related with the clubbing probably due to the severe inflammatory effects of smoking on the vascular endothelium all over the body, again. FPG may behave as a positive APR in mild inflammatory disorders such as IBS but as a negative APR in moderate and severe inflammatory disorders such as smoking, digital clubbing, and SCDs.

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Knowledge about Hypertension and its Associated Risk Factors among Saudi University Students in Riyadh City

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Abstract

Objectives: To determine the level of knowledge of hypertension and its associated risk factors among Saudi undergraduate students in the universities of Riyadh City.

Methods: A cross-sectional study was conducted among the students from 11 universities in Riyadh City. Convenience sampling was used, and the survey was not validated. The survey was distributed manually but collected electronically. It consisted of four sections: socio-demographics, risk factors, complications, and general statements.

Results: We analyzed 605 participants' data; the highest participation percentage was from King Saud University (14.1% of the total); 42.1% of the participants were from the health track, and 69.8% of the participants who had heard about hypertension described the source as their families. The highest level of knowledge was on the general statement section where 45% had good knowledge, and the lowest was on the complications section where 30% had good knowledge. The total level of good knowledge was 31.1%.

Conclusion: This study identifies some gaps in the knowledge of hypertension among undergraduate university students. Further research is advised to reach conclusive and more accurate data.

Key words: knowledge hypertension, risk factors, undergraduate students, Riyadh, Saudi Arabia

Introduction

Hypertension or high blood pressure is a consistent elevation in blood pressure. It is a result of two forces. The first is systolic pressure (left ventricle contraction) and the second is diastolic pressure (rest period between beats)(1). Hypertension is considered as a systolic pressure equal to or higher than 140 or diastolic pressure equal to or higher than 90 on more than two separate check-ups. Some physicians may consider a systolic pressure between 130 to 139 or a diastolic pressure between 80 and 89 to be hypertensive if there are other cardiac risk factors(2).

There are two main types of hypertension: primary (essential) hypertension and secondary hypertension(2). Essential hypertension is the most frequent type of hypertension in adults (95%) and is diagnosed when there is sustained elevation of BP greater than 140/90 mm Hg and when no etiology can be determined for the hypertension(3). Secondary hypertension (SH) is defined as "a form of hypertension with an identifiable cause and is generally considered to affect approximately 5–10% of all hypertensive patients"(4). An extensive review of the literature from multiple countries found a wide variation in secondary hypertension's estimated prevalence (2-20%). This variation could be due to the underlying causes, and the availability of adequate diagnostic resources (laboratory or imaging)(4).

A 2013 study found that the most common causes of secondary hypertension in adolescents were renal parenchymal, renovascular diseases and aortic coarctation. The same causes were thought to be the most common for adults as well, and recent studies showed that obstructive sleep apnea is more common. Endocrine disorders are also associated with hypertension, and the most common were primary aldosteronism, thyroid disorders, Cushing's syndrome and pheochromocytoma(5).

Hypertension has many associated risk factors which can be categorized into modifiable and non-modifiable risk factors. Non-modifiable risk factors include aging, gender (male) and race(6). Modifiable risk factors include smoking, obesity, unhealthy lifestyle and diet(7). Sufficient knowledge about some risk factors such as smoking and diet could lead to effective prevention of hypertension(8). There is relatively little research studying undergraduate students' knowledge about hypertension. One of these studies was done in Japan and found that there is a generational difference in the knowledge of hypertension and its risk factors between adolescents and elderly, favoring the latter(9). Another study found that young men have low levels of knowledge in Mongolia(10). A Polish study demonstrated that even when schools teach about hypertension and its risk factors, the level of awareness is still low and random(11). The levels of knowledge among adolescents is alarming worldwide particularly in the Middle East.

A study in the United Arab Emirates found that the level of knowledge about the risk factors of hypertension was 60% in medical entry students, and Arab students scored lower than non-Arabs(12). A comparison could be made between the previous paper and another study performed in the Seychelles Islands where the percentage of participants who recognized the association between obesity and salt with hypertension, was 71% and 96%, respectively. The latter study's population was 25-64 years old. However, the population was entering medical students in the first study showing that even with a percentage such as 60%, the level is still lower relative to other communities(12)(13).

Two studies were published in Saudi Arabia regarding the prevalence of hypertension. The first was in 2007, which showed that 26.25% of the population were hypertensive(14). The other was in 2017, and the prevalence was 36%(15). In 10 years, there was almost a 10% increase in the prevalence of hypertension in Saudi Arabia.

Due to the limited literature about the knowledge of young adults towards hypertension and its risk factors in Saudi Arabia, we conducted a survey to measure the level of knowledge of students from different Riyadh City universities about hypertension and its associated risk factors. Determining the level of knowledge of Saudi undergraduate students about hypertension and its risk factors could increase the attention of stakeholders, thus increasing the knowledge about hypertension among the target group. This may help reduce the incidence of hypertension and its complications.

Methods

This study aimed to assess the level of knowledge among Saudi undergraduate university students in Riyadh City aged between 18 and 30 years. There were 11 universities included: Dar Al Uloom University (DAU), Al Faisal University (FU), Imam Muhammad ibn Saud Islamic University (IMAMU), King Saud University (KSU), King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Princess Nourah Bint Abdul Rahman University (PNU), Prince Sultan University (PSU), Riyadh Elm University (REU), Saudi Electronic University (SEU), Almaarefa University (UM), and Al Yamamah University (YU). One university was excluded because we did not receive a response for permission to conduct data collection (Arab Open University, Riyadh branch (AOU)). This study collected a representative sample via convenience sampling from 6/2/2020 until 22/2/2020, and the questionnaire was distributed either by giving the students an electronic device to complete on the spot or by giving them a QR code to scan and complete it on their devices. The population size was 256,203 based on data from the Ministry of Education for the academic year 2018-2019 (numbers for 2019-2020 were not ready). The total number of responses was 777, but 605 remained after applying the exclusion criteria: non-Saudis, those older than 30, those younger than 18, and those with contradictory answers such as choosing nothing from the above and another answer.

The survey was not validated, and a pilot study was done on 29 students from different universities and tracks to check for completion time and comprehensibility. A few questions were edited based on the feedback.

The questionnaire was split into four sections: socio-demographics, risk factors, complications, and general statements.

The socio-demographic questions consisted of sex, age, nationality, university, track, whether they changed their track or not, were they ever diagnosed with hypertension, and have they ever heard about hypertension and how. The risk factors section and complications section both consisted of multiple-choice questions with correct and incorrect choices. Wrong choices were categorized as wrong if there were no papers about it or if it was proven to have no correlation (14)(16)(17)(18)(19)(20). The general questions section was a three-way Likert scale and had predetermined answers; some were correct and others were false (16)(14).

The proposal was approved by the ethical committee of King Saud University on 08/09/2019, and the project number was E-19-4405. All participants were asked for their consent and their data was kept anonymous. Statistical analysis was performed by SPSS version 21.0. The statistical tests used were frequencies and chi-squared analysis. The confidence level was 95%, and the confidence interval was 4%.

Results

There were 777 total responses, and 605 remained after following the exclusion criteria. Table I shows sociodemographic results. There were more male than female participants and the highest number of responses came from KSU (14.2% of the total responses). Students from the health track made up 42.1% of the responses. 8.1% of the total students were diagnosed as hypertensives. We found that 97.4% of the students had heard of hypertension, and 69.8% of them heard about it from their families.

Tables II, III, and IV show the frequency of each answer on the risk factors, complications, and general statement sections, respectively. The highest correct choice from each section was as follows: age (61.3%) as a risk factor, arrhythmia (62.6%) as a complication, and that you can prevent hypertension by exercising and losing weight (85.3%) as general knowledge. Among the wrong choices, the most frequent were panic attacks and anger (44.1%) as a risk factor, anemia as a complication (20.7%), and that a hypertensive must present with symptoms or else does not have the disease (36.9%).

Figures 1, 2, and 3 show the level of knowledge for each of the sections: risk factors, complications, and general statements section. The categorization was based on a 50% cut-off point. If the correct choices were more than 50% and the wrong choices were less than 50%, then they were considered to have good knowledge in that section. On the other hand, if they had fewer than 50% of the correct choices or more than 50% of the wrong choices, then they were considered to have poor knowledge. The highest level of knowledge was in the general statements section where 45% of the participants had good knowledge. The highest level of poor knowledge was in the complications section (65%).

To be considered knowledgeable in general, one should show good knowledge in two out of three sections, i.e., more than 50%. In total, 31.1% of the total students had good knowledge. Table V shows the levels of knowledge and how it was distributed by gender and track. Males were more knowledgeable than females, but this comparison was not significant. Track-based differences were highly significant. Students studying in the health track were more knowledgeable than their peers in the humanitarian and science tracks. Humanitarian students were the least knowledgeable with 84.4% of them having poor knowledge.

Table I: Sociodemographic section	N (%) 605 (100)
Gender	
Male	365 (60.3)
Female	240 (39.7)
University	
DAU	45 (7.4)
FU	32 (5.3)
IMAMU	82 (13.6)
KSU	86 (14.2)
KSAU-HS	67 (11.1)
PNU	54 (8.9)
PSU	47 (7.8)
REU	66 (10.9)
SEU	30 (5.0)
UM	53 (8.8)
YU	43 (7.1)
Track	
Humanitarian	109 (18.0)
Health	255 (42.1)
Science	241 (39.8)
Were you diagnosed with hypertension?	
No	556 (91.9)
Yes	49 (8.1)
Have you heard of hypertension?	
No	16 (2.6)
Yes	589 (97.4)
If yes, what was the source? *	
Family	422 (69.8)
Social media	298 (49.3)
School	289 (47.8)
Traditional media	153 (25.3)
Self-learning	250 (41.3)
From a doctor	151 (25.0)
Nothing (unanswered)	26 (4.3)

*Indicates that it is a multiple-choice question, so answers are not complementary.

Table II: Risk factors section	N (%)
Ethnicity (Caucasian, Asian)	119 (19.7)
Diabetes mellitus	225 (37.2)
Vascular diseases	261 (43.1)
Age	371 (61.3)
Smoking	313 (51.7)
Obesity	367 (60.7)
Kidney problems	122 (20.2)
Thyroid diseases	100 (16.5)
Pregnancy	101 (16.7)
Low physical activity	261 (43.1)
Gene and family history of hypertension	314 (51.9)
Excessive eating of salt	353 (58.3)
Drinking caffeine§	204 (33.7)
Insomnia§	131 (21.7)
Drinking excessive amounts of water§	19 (3.1)
Fever§	30 (5.0)
Panic attacks and anger§	267 (44.1)
Urine retention§	84 (13.9)
Nothing from the above	6 (1.0)

§ indicates that the choice is wrong

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Urine retention§	84 (13.9)
Nothing from the above	6 (1.0)

§ indicates that the choice is wrong

Table III: Complications section	N (%)
Cerebral stroke	280 (46.3)
Retinal hemorrhage	140 (23.1)
Arrhythmia	379 (62.6)
Sudden death	252 (41.7)
Peripheral vascular diseases (such as occlusion)	182 (30.1)
Heart failure	252 (41.7)
Aneurisms	205 (33.9)
Coronary vascular diseases	207 (34.2)
Alzheimer	18 (3.0)
Kidney diseases	149 (24.6)
Anemia§	125 (20.7)
Parkinson's disease§	47 (7.8)
Diabetes mellitus§	96 (15.9)
Nothing from the above	30 (5.0)

§ indicates that the choice is wrong

Table IV: General knowledge section. N (%)

	Agree	Neutral	Don't agree
A hypertensive must present with symptoms, else he does not have the disease§	223 (36.9)	240 (39.7)	142 (23.5)
Hypertension is a prevalent disease in Saudi Arabia	376 (62.1)	182 (30.1)	47 (7.8)
You can prevent hypertension by exercising and losing weight	516 (85.3)	77 (12.7)	12 (2.0)
People under 30 years old do not have hypertension or heart diseases§	41 (6.8)	138 (22.8)	426 (70.4)
Most hypertension cases do not feel any symptoms until a complication happens	256 (42.3)	246 (40.7)	103 (17.0)
Hypertension is one type, and it cannot be treated§	80 (13.2)	182 (30.1)	343 (56.7)
Cessation of smoking could help in preventing hypertension	469 (77.5)	114 (18.8)	22 (3.6)
No one could have hypertension unless they have a family history§	62 (10.2)	115 (19.0)	428 (70.7)

§ indicates that the choice is wrong

Table V: Total level of knowledge with comparisons.

	Level of Knowledge		P-value
	Poor Knowledge	Good Knowledge	
	N (%)	N (%)	
	417 (68.9)	188 (31.1)	
Gender			
Male	249 (68.2)	116 (31.8)	
Female	168 (70)	72 (30)	0.643
Track			
Humanitarian	92 (84.4)	17 (15.6)	
Health	143 (56.1)	112 (43.9)	<0.01
Science	182 (75.5)	59 (24.5)	

Discussion

To summarize, our study found that although many students have heard about the term “hypertension” by themselves or from a family member; their knowledge about it is insufficient and unsatisfactory. This indicates the need to transmit knowledge especially in an area with so many hypertensives. The research did not reveal any significant relationship between sex and level of knowledge about hypertension and its risk factors. Other related observations in this field varied (17)(18)(19); however, students in the health track had the highest level of knowledge followed by students in the science track.
Knowledge about individual aspects in the risk factors section was low relative to a study conducted in the United Arab Emirates (UAE) that had a similar population to ours. For example, the level of knowledge that diabetes mellitus is a risk factor was 37.2% compared to 50% in the UAE study(12). Knowledge about complications was pretty similar relative to prior work although the population was different. The level of knowledge about stroke was 46.3%, but in prior work was 46.2%(21). The results are similar in respect to knowledge about visual impairment and retinal hemorrhage.

By showing these low rates of knowledge about hypertension among young adults, our study underscores the need to focus on this population. There is a lack of adoption of raising awareness on such topics. This issue has also been repeatedly identified in knowledge, attitudes, and practice studies in the west(20)(22)(23). When individuals have background knowledge about hypertension’s risk factors, they guide the prevention of hypertension among them(8). This eventually leads to fewer cases of hypertension and hence a cessation of its complications.

This study does have some limitations. First, our study method was convenience sampling, which, while easy to conduct, may lead to selection bias. This obstacle could be overcome by performing a random sampling method instead. Even though the study assessed multiple risk factors and complications, we could not assess all of them. Enhancing those sections by choosing other specific risk factors and complications could offer a more precise understanding of the population’s knowledge of hypertension and may help to create better strategies to fight it. Data acquisition was via a questionnaire, which may lead to misinterpretation of questions that conflicts with the researcher’s main goal of the question, thus leading to inaccurate results during data analysis. Finally, our main intent was to reach a 3% confidence interval, but that goal was not met due to the SARS-CoV-2 pandemic and the shift towards online learning.

The knowledge about hypertension and its risk factors among the adolescent population has health implications for both hypertensives and non-hypertensives. This research showed that most of the participants’ knowledge about hypertension came from their families, followed by social media. This may be basic good knowledge but it is not always detailed nor precise. This highlights the need for the stakeholders to develop educational health programs. In addition, the implementation of educational hypertension sessions through social networks may be very helpful.

Conclusion

This study shows that there is a gap in the knowledge of hypertension across multiple different aspects. Although our sample may not be representative, a larger study is advised to reach a conclusive result for education that reduces the impact of hypertension.

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