World Family Medicine Journal
incorporating the Middle East Journal of Family Medicine

ISSN 1839-0188

June 2025 - Volume 23 Issue 4

Medical Situation in Gaza

Editorial

Chief Editor:
A. Abyad
MD, MPH, AGSF, AFCHSE
Email::
aabyad@cyberia.net.lb
Mobile: 961-3-201901

Publisher
Lesley Pocock
medi+WORLD International
AUSTRALIA
Email:
lesleypocock@mediworld.com.au
publishermwi@gmail.com

The convergence of chronic diseases, environmental health challenges, and social determinants of health in the Middle East underscores the urgent need for integrated, culturally tailored public health strategies. The six manuscripts presented in this issue offer valuable insights into diverse healthcare challenges ranging from metabolic and hematological disorders to gynecological malignancies and medication adherence. Together, they highlight systemic gaps but also point to promising, evidence-based pathways for improvement.

The paper by Alghamdi et al. on diabetes outcomes in Saudi primary health centers reveals that only 30% of patients achieve glycemic control, with high rates of complications such as dyslipidemia and retinopathy. These data reinforce the critical importance of strengthening the role of primary healthcare providers in chronic disease monitoring and lifestyle counseling, especially in populations burdened by obesity and hypertension.

In parallel, Abdelmageed and colleagues explore the environmental dimension of healthcare through their quality improvement project on green prescribing. Their findings—that switching from metered-dose to dry powder inhalers maintained disease control in most patients—demonstrate the potential for environmentally sustainable practices to coexist with effective clinical care. This innovation, rooted in global climate responsibility, should inform national respiratory guidelines.

Addressing nutritional determinants of disease, the study on iron deficiency anemia (IDA) among children in Jeddahpaints a concerning picture of inadequate dietary practices and low parental awareness. Given that IDA impairs cognitive development and academic performance, the authors rightly call for intensified maternal education campaigns, aligned with pediatric nutritional surveillance.

The burden of gynecological cancers, as documented in Hadhramout, Yemen, further illustrates the regional disparities in screening and early diagnosis. With ovarian and cervical cancers comprising over 70% of cases and increasing incidence trends, this retrospective study urges policymakers to invest in HPV vaccination, public awareness, and infrastructure for gynecological oncology.

Meanwhile, the study on antihypertensive medication adherence in Saudi patients reveals that nonadherence stems from multifactorial causes—ranging from side effects to poor patient-pharmacist communication. Notably, it elevates the role of pharmacists as educators and support providers in blood pressure control, suggesting a shift toward team-based chronic care models.

Finally, the manuscript by Helvaci et al. challenges conventional transfusion practices in sickle cell disease, advocating for more conservative use of red blood cell transfusions. The authors provide a compelling rationale for prioritizing hydroxyurea therapy and reserving transfusions for acute crises, thereby minimizing alloimmunization risks. This aligns with global calls for more judicious use of transfusion resources.

Collectively, these six studies converge on key themes: the necessity of health system strengthening, the value of prevention, the power of patient education, and the imperative for locally driven research. Whether through technological innovation, nutritional reform, pharmaceutical stewardship, or cancer surveillance, each paper contributes to a vision of primary and public health that is not only responsive but proactive.

As the Middle East faces rising burdens of non-communicable diseases, aging populations, and climate-induced health threats, this body of work affirms that contextualized, evidence-based interventions are central to improving outcomes. The path forward must be interdisciplinary, patient-centered, and rooted in robust primary care systems.

Warm regards,
Dr. Abdulrazak Abyad
Editor-in-Chief
Middle East Journal of Family Medicine

Petition For Peace - Send UN Peacekeepers To Palestine

This is the Gaza-Palestine plan of the Arab League, the UN, and the EU:

"The recovery and reconstruction of Gaza should not wait"

Sigrid Kaag UN Senior Humanitarian and Reconstruction Coordinator for the Strip said, emphasizing the need for education, healthcare, housing, in addition to establishing governance and security arrangements.

It is clear that Israel and the US must cease and desist, comply with international laws, and get out of the way of the rest of the world to save the citizens of Gaza and all of Palestine and to rebuild their nation.
The Arab League has called upon the UN to be one of the leaders in an overall plan for Gaza, as it has also called upon the EU and the Palestinian

Kaja Kallas, High Representative for Foreign Affairs and Security Policy/ Vice-President of the European Commission announced a multiannual programme for Palestinian recovery and resilience worth up to â‚¬1.6 billion and stated, " The EU is determined to support the Palestinian Authority in its reform efforts. The Comprehensive Programme for Palestine is designed to promote greater Palestinian control, autonomy, and capacity. The EU remains firmly committed to the Two-State solution, as the only way to achieve sustainable peace and security for Israel, the Palestinians, and the region. "

It is clear that both Israel and Hamas give up any designs to govern Gaza and that Israel give up its designs on and occupation of the Wes Bank and East Jerusalem, including relocating all illegal Israeli settlers from Palestinian Territory.

Among the breaches of international law, the International Justice Court identified practices such as: forcible evictions; pervasive house demolitions and restrictions on residence and movement; the transfer and retention of settlers into East Jerusalem and the West Bank; the failure to protect Palestinians from settler violence; placing restrictions on access to water; the extension of Israeli law into the West Bank and East Jerusalem; and the exploitation by Israel of resources in the occupied territories.

Per the ICJ decision, every nation has a duty to not only suspend all forms of support for the state of Israel that enables it to maintain the unlawful occupation, but to also prohibit any and all of their citizens and entities from "rendering aid or assistance" toward maintaining Israel's presence in the occupied territories.

Rule 135 of the 2005 ICRC customary IHL study prescribes that "children affected by armed conflict are entitled to special respect and protection" in international and non-international armed conflicts.

The 1949 Geneva Conventions and their 1977 Additional Protocols establish that "children shall be the object of special respect and shall be protected against any form of indecent assault. The parties to the conflict shall provide them with the care and aid they require" (API Art.77). They center the provisions for the protection of children on several main objectives-namely sheltering them from hostilities; maintaining family unity; and ensuring the necessary care, relief, or protection for those caught in hostilities.

Robyn Austin
Canada

(from her Facebook Post)

Diabetes Outcomes in Saudi Arabia: A Nationwide Assessment of Glycemic Control and Complications in Primary Health Centers

Riyadh Abdullah Ali Alghamdi [1], Faisal Yehia Almalky [2], Abdulelah Abdulghani Thigah [3], Ghaida Hamoud Hamed Alosaimi [4], Shahad Abdullah Tael Alsuwat [4]

[1] Family medicine Consultant, Saudi fellowship program of diabetes, Al Noor Specialist Hospital, Makkah, KSA
[2] Consultant of internal medicine and adult endocrinology, Alnoor specialist hospital Makkah, KSA
[3] Diabetes Fellow at King Abdulaziz University Hospital, Family medicine Consultant
[4] Family medicine resident, family medicine academy, Makkah, Saudi Arabia

Corresponding author:
Riyadh Abdullah Ali Alghamdi
Family medicine Consultant, Saudi fellowship program of diabetes, Al Noor Specialist Hospital, Makkah, KSA
Email: moad3_1986@outlook.sa

Received: April 2025. Accepted: May 2025; Published:June 1, 2025.
Citation: Riyadh Abdullah Ali Alghamdi et al. Diabetes Outcomes in Saudi Arabia: A Nationwide Assessment of Glycemic Control and Complications in Primary Health Centers. World Family Medicine. June 2025; 23(4): 6 - 13. DOI: 10.5742/MEWFM.2025.795257866

Abstract

Background: Diabetes mellitus poses a significant public health challenge in Saudi Arabia, with rising prevalence and complications burden. Primary healthcare centers (PHCs) serve as frontline providers, yet data on diabetes outcomes in these settings remains limited.

Objective: This study aimed to evaluate glycemic control status, complication patterns, and predictors of poor outcomes among diabetic patients attending PHCs in Saudi Arabia.

Methods: A cross-sectional study was conducted among 312 diabetic patients (T1DM=22; T2DM=290) across Saudi PHCs. Data on demographic characteristics, glycemic control (HbA1c <7% as controlled), and complications (dyslipidemia, retinopathy, neuropathy, etc.) were collected through medical records and clinical assessments. Logistic regression identified predictors of complications.

Results: The study found that only 30.4% of patients achieved adequate glycemic control, with no significant difference between those with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) (27.3% vs. 30.7%, p=0.737). Dyslipidemia emerged as the most prevalent complication, affecting 42.3% of the overall cohort, and was significantly more common among T2DM patients compared to those with T1DM (45.2% vs. 4.5%, p=0.001). Retinopathy was observed in 13.4% of T2DM patients, while no cases were reported among those with T1DM (p=0.049). Furthermore, obesity (OR=4.74), hypertension (OR=5.21), and poor glycemic control (OR=4.35) were found to be strong predictors of diabetes-related complications, all with statistically significant associations (p=0.001).
Conclusion: The study reveals alarmingly poor glycemic control and high complication rates in Saudi PHCs, driven by modifiable risk factors. Urgent interventions targeting obesity, hypertension, and glucose management are needed to improve diabetes outcomes.

Keywords
Diabetes mellitus, complications, glycemic control, primary healthcare, Saudi Arabia

Introduction

Diabetes mellitus has become one of the most pressing public health challenges of the 21st century, with its global prevalence rising to epidemic levels [1]. The disease featured by chronic hyperglycemia resulting from defects in insulin secretion, action, or both, leads to serious damage to multiple organ systems over time [2]. The World Health Organization estimates that diabetes directly caused 1.5 million deaths worldwide in 2019, with the Eastern Mediterranean region experiencing particularly rapid increases in disease burden [3, 4]. Saudi Arabia has been disproportionately affected, with age-adjusted prevalence rates among adults reaching 18.3%, nearly double the global average, according to recent International Diabetes Federation reports [5]. This metabolic disorder exists in two primary forms: type 1 diabetes (T1DM), an autoimmune condition typically diagnosed in childhood, and type 2 diabetes (T2DM), which accounts for 90-95% of cases and is strongly associated with obesity and lifestyle factors [6].

The progressive nature of diabetes frequently leads to devastating complications that significantly reduce quality of life and increase mortality. Chronic hyperglycemia triggers pathological changes in both microvascular and macrovascular systems, resulting in retinopathy, nephropathy, neuropathy, and accelerated cardiovascular disease [7]. Microvascular complications particularly affect the eyes, kidneys, and nerves, with diabetic retinopathy the leading cause of blindness in working-age adults globally [8]. Macrovascular complications manifest as atherosclerotic changes, increasing risks of coronary artery disease, stroke, and peripheral vascular disease by two- to four-fold [9]. Alarmingly, recent Saudi national data indicates that approximately 40-50% of diabetic patients already show evidence of complications at diagnosis, highlighting the need for earlier detection and intervention [10]. Within the Saudi healthcare system, primary health care centers (PHCs) serve as the first line of defense against diabetes and its complications. This study aims to broadly evaluate diabetes-related outcomes among patients attending primary healthcare centers (PHCs) in Saudi Arabia.

Methodology

A cross-sectional study was conducted to assess diabetes-related outcomes and associated factors among diabetic patients attending primary health care centers in Saudi Arabia. The study included adult patients aged 18 years and above with a confirmed diagnosis of type 1 or type 2 diabetes mellitus who were attending scheduled follow-up visits. Patients with gestational diabetes or incomplete medical records were excluded. A total of 312 patients were recruited using a consecutive sampling technique. Data collection was performed through structured interviews and a review of patients' medical records. Information was gathered on sociodemographic characteristics, clinical factors (type of diabetes mellitus, presence of hypertension, obesity status, and type of visit), diabetes-related complications (including dyslipidemia, peripheral neuropathy, retinopathy, proteinuria, diabetic foot, and other complications), and blood glucose control status. Blood glucose control status was determined based on the latest available HbA1c results. The primary outcomes assessed were the presence of diabetes-related complications, while secondary outcomes included blood glucose control status and referral status to specialized care. Ethical approval for the study was obtained and written informed consent was secured from all participants. Confidentiality and anonymity were maintained throughout the study period.

Data analysis

The data were collected, reviewed, and then fed into Statistical Package for Social Sciences version 26 (Released 2019, Armonk, NY: IBM Corp). Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. For categorical variables, Pearson's chi-square (χ^2) test was used to assess differences in proportions between groups, with exact probability tests applied when necessary. For continuous variables, such as age, comparisons between groups were made using independent t-tests, with the significance level set at $p < 0.05$. To identify potential predictors of complications among diabetic patients, logistic regression analysis was conducted. This model included factors such as age, gender, type of diabetes, obesity, hypertension, and glycemic control. The odds ratios (ORAs) and 95% confidence intervals (CIs) were calculated to estimate the strength and direction of associations, and statistical significance was determined based on p-values less than 0.05. All statistical analyses were performed using statistical software, and results were considered statistically significant if $p < 0.05$.

Results

Among the total study population of 312 diabetic patients, the majority were diagnosed with type 2 diabetes mellitus (T2DM) (n = 290, 93.0%), while only a small proportion had type 1 diabetes mellitus (T1DM) (n = 22, 7.1%). Age distribution showed a statistically significant difference between the two groups (p = .001). Most T1DM patients (86.4%) were between 18–30 years, while T2DM patients were predominantly older, with 35.2% aged 51–60 years and 43.1% above 60 years. The mean age for T1DM patients was 24.4 ± 4.7 years compared to 58.7 ± 11.8 years for T2DM. Regarding gender, males represented a slightly higher proportion overall (55.1%), with similar distributions in both T1DM (50.0%) and T2DM (55.5%) groups (p = .616). Obesity was reported in 44.2% of participants, affecting 36.4% of those with T1DM and 44.8% with T2DM, with no significant difference (p = .441). Hypertension (HTN) showed a statistically significant association with diabetes type (p = .002), being more prevalent in the T2DM group (37.2%) and rare among T1DM patients (4.5%). All patients (100%) were attending follow-up visits at the time of data collection.

Table 1. Sociodemographic and Clinical Characteristics of Diabetic Patients by Type of Diabetes Mellitus (N=312)

Data	Total (N=312)		Type of DM				p-value
			T1DM (N=22)		T2DM (N=290)		
	No	%	No	%	No	%	
Age in years							
18-30	19	6.1%	19	86.4%	0	0.0%	.001*^
31-40	20	6.4%	3	13.6%	17	5.9%	
41-50	46	14.7%	0	0.0%	46	15.9%	
51-60	102	32.7%	0	0.0%	102	35.2%	
> 60	125	40.1%	0	0.0%	125	43.1%	
Mean ± SD	56.2 ± 14.5		24.4 ± 4.7		58.7 ± 11.8		
Gender							
Male	172	55.1%	11	50.0%	161	55.5%	.616
Female	140	44.9%	11	50.0%	129	44.5%	
Obesity							
Yes	138	44.2%	8	36.4%	130	44.8%	.441
No	174	55.8%	14	63.6%	160	55.2%	
HTN							
Yes	109	34.9%	1	4.5%	108	37.2%	.002*
No	203	65.1%	21	95.5%	182	62.8%	
Type of Visit							-
Follow up	312	100.0%	22	100.0%	290	100.0%	

P: Pearson X2 test ^: Exact probability test * P < 0.05 (significant)

Figure 1 illustrates blood glucose control status between patients with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Overall, 30.4% (n = 95) of the total 312 patients had controlled blood glucose levels, while 69.6% (n = 217) had uncontrolled levels. Among T1DM patients, only 27.3% (n = 6) had controlled glucose levels compared to 30.7% (n = 89) in the T2DM group. The majority of both T1DM (72.7%, n = 16) and T2DM (69.3%, n = 201) patients had uncontrolled blood glucose (P=.737).

Figure 1. Blood Glucose Control Status by Type of Diabetes Mellitus among Study Patients (N=312)

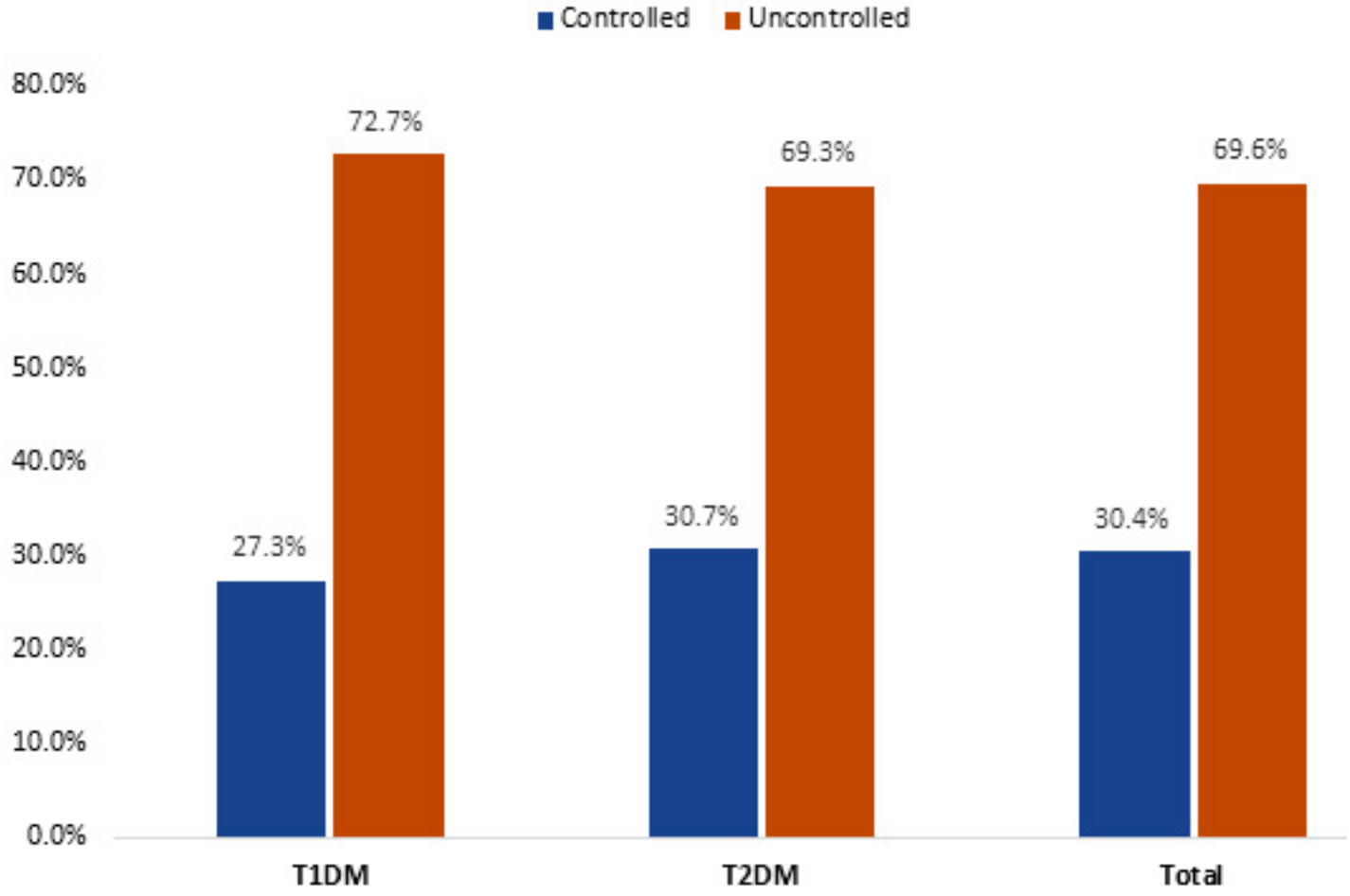


Table 2 presents diabetes-related outcomes among patients with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Overall, dyslipidemia was the most common complication, observed in 42.3% of patients, and was significantly more prevalent in the T2DM group (45.2%) compared to only 4.5% in the T1DM group (p = .001). Retinopathy was also significantly associated with T2DM (13.4%) and was absent among T1DM patients (p = .049). Other complications such as peripheral neuropathy (15.7%), proteinuria (9.9%), diabetic foot (17.0%), and other unspecified complications (1.3%) showed no statistically significant differences between the two groups. Notably, proteinuria appeared more frequently in T1DM patients (18.2%) than in T2DM (9.3%), though this difference did not reach statistical significance (p = .180). These findings highlight the higher burden of certain complications, particularly dyslipidemia and retinopathy, among patients with T2DM.

Table 2. Diabetes-Related Outcomes by Type of Diabetes Mellitus among Study Patients (N=312)

Complications	Total (N=312)		Type of DM				p-value
			T1DM (N=22)		T2DM (N=290)		
	No	%	No	%	No	%	
Dyslipidemia	132	42.3%	1	4.5%	131	45.2%	.001*
Peripheral Neuropathy	49	15.7%	2	9.1%	47	16.2%	.376^
Retinopathy	39	12.5%	0	0.0%	39	13.4%	.049*^
Proteinuria	31	9.9%	4	18.2%	27	9.3%	.180
Diabetic Foot	53	17.0%	2	9.1%	51	17.6%	.306
Other complications	4	1.3%	0	0.0%	4	1.4%	.579^

P: Pearson X2 test ^: Exact probability test * P < 0.05 (significant)

Figure 2 shows the referral status of patients based on the type of diabetes mellitus. Among the total sample, the vast majority (98.7%, n = 308) were not referred to secondary or tertiary care centers, while only 1.3% (n = 4) of patients were referred. All patients with type 1 diabetes mellitus (T1DM) (100%, n = 22) were managed without referral, whereas a small proportion of type 2 diabetes mellitus (T2DM) patients (1.4%, n = 4) required referral.

Figure 2. Referral Status of Diabetic Patients by Type of Diabetes Mellitus (N=312)

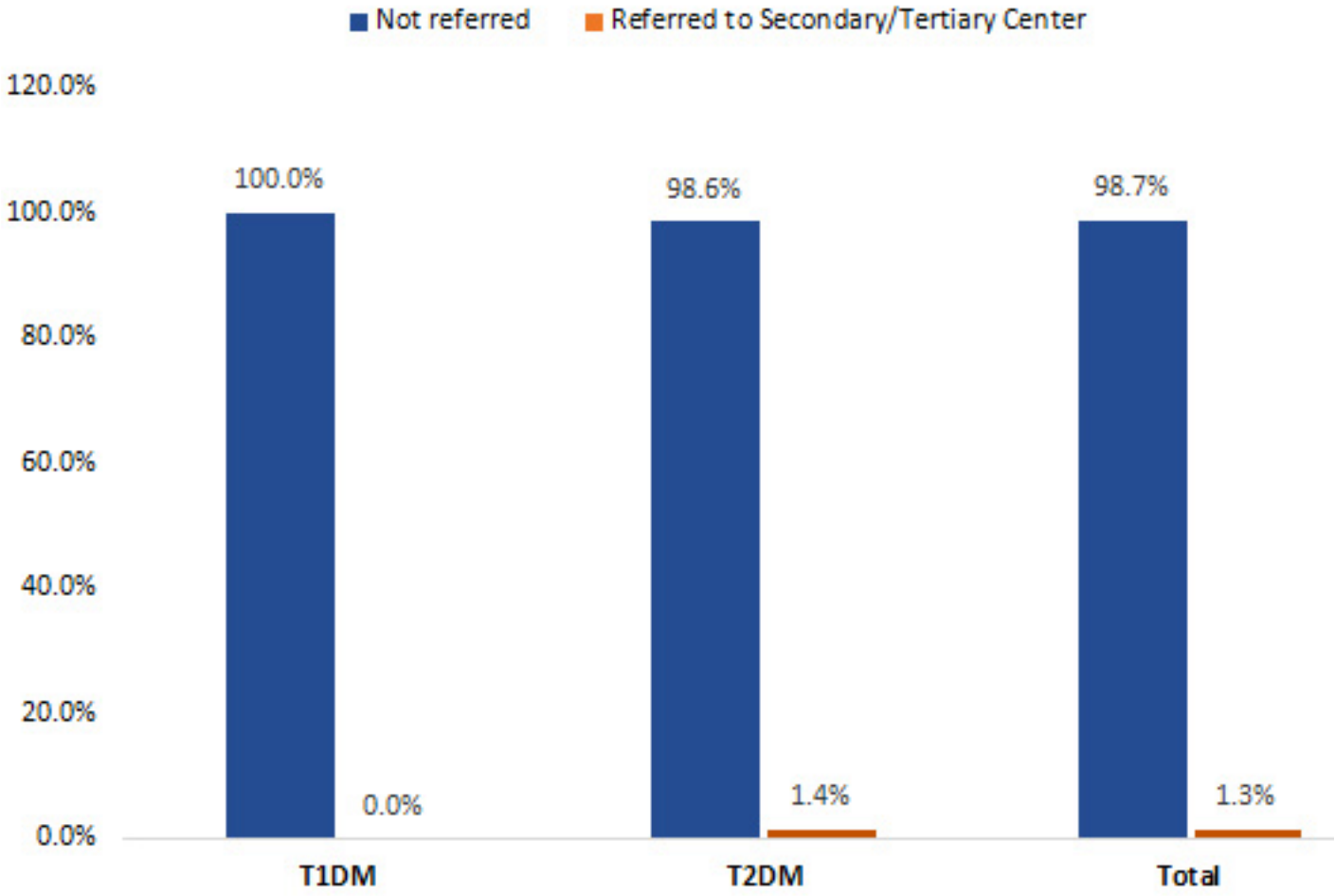


Table 3 outlines the results of the logistic regression analysis for predictors of complications among diabetic patients. Several factors were found to significantly predict complications. Obesity, hypertension (HTN), and uncontrolled diabetes mellitus (DM) all had strong associations with an increased likelihood of complications. Obesity [ORA = 4.74, p = .001], HTN (ORA = 5.21, p = .001), and uncontrolled DM (ORA = 4.35, p = .001) were identified as significant predictors, with ORAs indicating a substantially higher risk of complications in these groups. Age, gender, and type of diabetes (T1DM vs. T2DM) were not statistically significant.

Table 3. Logistic regression analysis for predictors of complications among diabetic patients

Factors	Sig.	OR_A	95% CI	
			Lower	Upper
Age in years	.973	1.10	.74	1.99
Male gender	.239	1.38	.81	2.34
Type II DM	.181	2.45	.66	9.15
Obesity	.001*	4.74	2.55	8.81
HTN	.001*	5.21	2.75	9.89
Uncontrolled DM	.001*	4.35	2.21	8.55

ORA: Adjusted odds ratio CI: Confidence interval * P < 0.05 (significant)

Discussion

The study assessed diabetes-related outcomes and complications among patients at PHCs in Saudi Arabia. The clear age difference between T1DM and T2DM patients supports established evidence regarding their distinct etiologies, T1DM typically appearing in younger individuals due to its autoimmune origin, while T2DM is more prevalent in older adults. Also, gender distribution showed no significant differences, separating from some regional studies that report a higher prevalence of T2DM among Saudi males [11]. However, this matches the global trends suggesting a narrowing gender gap in diabetes prevalence as lifestyle risk factors become more evenly distributed between sexes [12]. The similar obesity rates across T1DM and T2DM groups challenge traditional associations of obesity with T2DM alone and may reflect increasing obesity levels in Saudi Arabia, even among the youth, which is a growing concern [13, 14]. Likewise, the strong correlation between hypertension and T2DM in this study is consistent with existing literature highlighting the main role of metabolic syndrome in T2DM progression [15, 16]. On the other hand, the low prevalence of hypertension in T1DM patients may be attributed to the younger age group's relatively better cardiovascular profiles, though this may change with time, warranting ongoing monitoring. The universal adherence to follow-up visits in our cohort is notable and differs from the lower retention rates reported in other settings [17]. This could reflect improved patient engagement in Saudi PHCs, possibly driven by the Saudi Vision 2030 health initiatives that emphasize enhanced chronic disease care and patient-centered primary health services [18].

Regarding diabetes control, our study reveals considerable challenges in achieving glycemic control among diabetic patients in Saudi PHCs, with most cases showing uncontrolled blood glucose levels and no significant difference observed between T1DM and T2DM patients. This reflects previous Saudi findings, such as Al-Rubeaan's (2015) national survey showing only 30% of patients reaching HbA1c targets [19]. Interestingly, the similar rates of poor control between T1DM and T2DM differ from international studies like Foster et al. (2019), which reported worse control in T1DM due to insulin management complexities [20], but align with regional data from Alqurashi et al. (2011) [21]. Several factors may explain these patterns. Challenges within the Saudi healthcare system, such as fragmented services and insufficient patient education, have been documented by Alotaibi et al. (2017) [14]. Additionally, cultural and lifestyle factors, including high-calorie diets and sedentary behavior, remain significant contributors according to the IDF Diabetes Atlas (2021) [22]. The lack of difference in control rates across diabetes types suggests the need for both universal and tailored interventions. For T1DM patients, enhancing insulin management and improving carbohydrate-counting skills is critical, as highlighted by Alaqeel et al. (2019) [23]. For T2DM patients, strengthening medication adherence and lifestyle interventions is vital, consistent with American Diabetes Association (2023) recommendations [24].

Also, our study reveals critical patterns in diabetes-related complications among patients attending primary healthcare centers in Saudi Arabia, with notable differences between T1DM and T2DM populations. The significantly higher prevalence of dyslipidemia in T2DM patients is similar to the metabolic profile of type 2 diabetes and reflects findings from the SAUDI-DM study, which identified dyslipidemia as the most common comorbidity in Saudi diabetic patients [19]. This strong association indicates the importance of regular lipid monitoring and management in T2DM care protocols within primary health settings. The complete absence of retinopathy in our T1DM cohort contrasted with its significant presence in T2DM patients may reflect differences in disease duration and glycemic control patterns between the groups, consistent with observations by Al Hayek et al. in Saudi populations [25]. The relatively high prevalence of peripheral neuropathy and diabetic foot complications across both diabetes types, without significant intergroup differences, suggests these outcomes may be more related to long-term glycemic control than to diabetes etiology itself. This finding supports the American Diabetes Association's emphasis on comprehensive foot care for all diabetic patients regardless of type [24]. The trend toward higher proteinuria in T1DM patients, though not statistically significant, warrants attention as it may indicate early renal involvement in younger patients, a pattern noted in some regional studies [26] but requiring further investigation.

The logistic regression analysis indicates that modifiable risk factors, specifically obesity, hypertension, and uncontrolled diabetes, are the strongest predictors of complications among diabetic patients. These findings highlight that metabolic and comorbid conditions have a greater impact on complication risk than demographic factors like age or diabetes type, aligning with the International Diabetes Federation's focus on managing cardiovascular risk factors but differing from studies that identified age as a predictor [24, 27].

Conclusions and Recommendations

In conclusion, the current study showed significant challenges in diabetes management and complications among patients in Saudi primary healthcare centers. The high prevalence of uncontrolled blood glucose and frequent diabetes-related complications, particularly dyslipidemia and retinopathy in T2DM patients, underlines gaps in current care approaches. The strong association between modifiable risk factors (obesity, hypertension, and poor glycemic control) and complications emphasizes the need for targeted interventions. Key recommendations include: (1) implementing regular complication screening protocols in PHCs, especially for retinopathy and dyslipidemia; (2) developing intensive lifestyle and medication programs targeting obesity and hypertension; (3) enhancing diabetes education to improve glycemic control; and (4) establishing standardized monitoring systems for high-risk patients. These measures should be integrated into Saudi Arabia's primary care diabetes programs to reduce complications and improve long-term outcomes.

References

1. Standl E, Khunti K, Hansen TB, Schnell O. The global epidemics of diabetes in the 21st century: Current situation and perspectives. European journal of preventive cardiology. 2019 Dec 1;26(2_suppl):7-14.
2. Sarkar BK, Akter R, Das J, Das A, Modak P, Halder S, Sarkar AP, Kundu SK. Diabetes mellitus: A comprehensive review. Journal of Pharmacognosy and Phytochemistry. 2019;8(6):2362-71.
3. World Health Organization. Diabetes fact sheet. Geneva: WHO; 2021.
4. Moradinazar M, Babakhani M, Rostami R, Shakiba M, Moradi A, Shakiba E. Epidemiological status of type 2 diabetes mellitus in the Middle East and North Africa, 1990-2019. Eastern Mediterranean Health Journal. 2022 Jul 1;28(7).
5. Bahijri SM, Jambi HA, Al Raddadi RM, Ferns G, Tuomilehto J. The prevalence of diabetes and prediabetes in the adult population of Jeddah, Saudi Arabia-a community-based survey. PloS one. 2016 Apr 1;11(4): e0152559.
6. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman medical journal. 2012 Jul;27(4):269.
7. Forbes JM, Cooper ME. Mechanisms of diabetic complications. Physiological reviews. 2013 Jan;93(1):137-88.
8. Ting DS, Tan KA, Phua V, Tan GS, Wong CW, Wong TY. Biomarkers of diabetic retinopathy. Current diabetes reports. 2016 Dec; 16:1-5.
9. Low Wang CC, Hess CN, Hiatt WR, Goldfine AB. Clinical update: cardiovascular disease in diabetes mellitus: atherosclerotic cardiovascular disease and heart failure in type 2 diabetes mellitus–mechanisms, management, and clinical considerations. Circulation. 2016 Jun 14;133(24):2459-502.
10. Abdulaziz Al Dawish M, Alwin Robert A, Braham R, Abdallah Al Hayek A, Al Saeed A, Ahmed Ahmed R, Sulaiman Al Sabaan F. Diabetes mellitus in Saudi Arabia: a review of the recent literature. Current diabetes reviews. 2016 Dec 1;12(4):359-68.
11. Al Dawish MA, Robert AA. Diabetes Mellitus in Saudi Arabia: challenges and possible solutions. In Handbook of healthcare in the Arab world 2021 Aug 11 (pp. 1083-1100). Cham: Springer International Publishing.
12. Forouhi NG, Luan J, Hennings S, Wareham NJ. Incidence of type 2 diabetes in England and its association with baseline impaired fasting glucose: the Ely study 1990–2000. Diabetic medicine. 2007 Feb;24(2):200-7.
13. Purnell JQ, Zinman B, Brunzell JD. The effect of excess weight gain with intensive diabetes mellitus treatment on cardiovascular disease risk factors and atherosclerosis in type 1 diabetes mellitus: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC) study. Circulation. 2013 Jan 15;127(2):180-7.
14. Alotaibi A, Perry L, Gholizadeh L, Al-Ganmi A. Incidence and prevalence rates of diabetes mellitus in Saudi Arabia: An overview. Journal of epidemiology and global health. 2017 Jan;7(4):211-8.
15. Alqubali HF, Albalawi KA, Alswat AE, Aljebreen AA, Alotaib KE, Aljehani HS, Almughamsi RA, Hussain AM, Albiek HF. Prevalence of type 2 diabetes mellitus and hypertension in overweight and obese people in Riyadh city, KSA 2017. The Egyptian Journal of Hospital Medicine. 2017 Oct 1;69(6):2614-7.
16. Salman RA, Al-Rubeaan KA. Incidence and risk factors of hypertension among Saudi type 2 diabetes adult patients: an 11-year prospective randomized study. Journal of Diabetes and its Complications. 2009 Mar 1;23(2):95-101.
17. Alwakeel JS, Al-Suwaida A, Isnani AC, Al-Harbi A, Alam A. Concomitant macro and microvascular complications in diabetic nephropathy. Saudi journal of kidney diseases and transplantation. 2009 May 1;20(3):402-9.
18. Saudi Vision 2030. Health Sector Transformation Program. Riyadh, Saudi Arabia; 2021.
19. Al Rubeaan K, Al□Manaa HA, Khoja TA, Ahmad NA, Al Sharqawi AH, Siddiqui K, Alnaqeb D, Aburisheh KH, Youssef AM, Al Batel A, Alotaibi MS. Epidemiology of abnormal glucose metabolism in a country facing its epidemic: SAUDI□DM study: SAUDI□DM. Journal of diabetes. 2015 Sep;7(5):622-32.
20. Foster NC, Beck RW, Miller KM, Clements MA, Rickels MR, DiMeglio LA, Maahs DM, Tamborlane WV, Bergenstal R, Smith E, Olson BA. State of type 1 diabetes management and outcomes from the T1D exchange in 2016–2018. Diabetes technology & therapeutics. 2019 Feb 1;21(2):66-72.
21. Alqurashi KA, Aljabri KS, Bokhari SA. Prevalence of diabetes mellitus in a Saudi community. Annals of Saudi medicine. 2011 Jan;31(1):19-23.
22. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels, Belgium; 2021.
23. Alaqeel AA. Pediatric diabetes in Saudi Arabia: Challenges and potential solutions. A review articles. International Journal of Pediatrics and Adolescent Medicine. 2019 Dec 1;6(4):125-30.
24. American Diabetes Association. Standards of medical care in diabetes-2023. Diabetes Care. 2023;46(Suppl 1): S1-S207.
25. Al Hayek A, Al Dawish MA. Technology for the Management of Type 1 Diabetes Mellitus in Saudi Arabia and MENA Region: A Systematic Review. Current Diabetes Reviews. 2025 Jul;21(6): E260424229416.
26. Al-Zahrani N, AlSwat HK, AlQarni AM, Alzahrani SS, Boubshait LA, Alassaf LA, Alsalman Z. Prevalence and Risk Factors of Diabetic Nephropathy Among Saudi Type-1 Diabetic Patients in Taif City, Saudi Arabia. Diabetes, Metabolic Syndrome and Obesity. 2023 Dec 31:3609-16.
27. Shamshirgaran SM, Mamaghanian A, Aliasgarzadeh A, Aiminisani N, Iranparvar-Alamdari M, Ataie J. Age differences in diabetes-related complications and glycemic control. BMC endocrine disorders. 2017 Dec; 17:1-7.

Nutritional Habits of Children with Iron Deficiency Anemia in Jeddah City: A Cross-sectional Study

Moufag Mohammed Saeed Tayeb

Correspondence:
Moufag Mohammed Saeed Tayeb
Consultant, Associate Professor Family Medicine
Faculty of Medicine – University of Jeddah, Saudi Arabia, Postal code: 23218
Mobile: +966-555517123
Telephone and fax number: 00966-125357773
Postal address: Makkah 24225
Email: (official) mmtayeb@uj.edu.sa; (personal): moufagta@yahoo.com,

Received: April 2025. Accepted: May 2025; Published:June 1, 2025.
Citation: Moufag Mohammed Saeed Tayeb. Nutritional Habits of Children with Iron Deficiency Anemia in Jeddah City: A Cross-sectional Study. World Family Medicine. June 2025; 23(4): 14 - 25. DOI: 10.5742/MEWFM.2025.795257867

Abstract

Background: Iron deficiency anemia (IDA) in children is primarily caused by poor nutritional habits.

Objective: This study investigated the nutritional habits of children with IDA in Jeddah city.

Methods: This cross-sectional study used a multiple-choice Arabic language electronic questionnaire on Google Forms about the nutritional habits of 120 children with IDA (71 boys and 49 girls) in Jeddah city. T he mothers of the affected children answered a questionnaire in a private clinic. They were asked about iron-rich foods from animals, vegetables, fruits, and legumes. Multiple choices were divided into five stages: small (0%–20%), few (20%–40%), middle (40%–60%), moderate (60%–80%), and huge (80%–100%).

Results: Consumption of foods high in iron was low, whereas consumption of low-quality foods was high. Consumption as follows: animal sources (eggs and red meats in moderate quantities, followed by fish, salmon, and tuna in middle quantities), vegetable sources (tomato) only in moderate quantities, and fruit sources (apples, watermelons, and bananas in moderate quantities, followed by berries in middle quantities).

Conclusions: In Jeddah city, children with IDA do not eat foods high in iron but consume several low-quality foods. Most legume and vegetable sources of iron are not consumed except for a few ones (lentils and tomatoes). Seafood and animal livers are not consumed. Cow's milk is the only type of food that is consumed in large quantities. The good news is that fruits are consumed in sufficient quantities. Therefore, IDA in children is primarily caused by poor dietary habits. Mothers must be educated about the consumption of foods high in iron in children, consumption of iron-fortified foods or milk formulas in early infancy, regular clinic visits, avoiding exclusive breastfeeding, starting oral iron at 4–6 months of age, weaning foods high in iron, and consuming artificial cow's milk in small quantities only.

Keywords: anemia, nutrition, iron, ferritin, children

Introduction

Red blood cells synthesis by bone marrow is called erythropoiesis and it is dependent on the presence of iron. The main source of iron is food and in its absorption from intestines; enterocytes absorb iron then transfer it to bone marrow by transferrin. This is the normal homeostasis of iron. However, in an iron deficiency state the amount of iron transferred to bone marrow is less and RBCs synthesis will also be less. Iron plays a role in transferring oxygen from the lungs to tissues because it is carried by red blood cells. This indicates that Iron Deficiency Anaemia (IDA) causes a lack of oxygen transfer to tissues. This will affect the child's growth and causes pallor, fatigue, rapid breathing, and frequent infections, as in Figure1.

The causes of hypochromic anemia in children differ according to age. Anemia in children <2 years is mainly caused by IDA, whereas anemia in schoolchildren is possibly due to other causes, such as thalassemia or celiac disease. In girls aged 11–18 years, IDA is mostly attributed to heavy menstrual cycles. The prevalence rate of anemia in children aged <2 years is 10.11%, and this is mostly due to IDA. In contrast, its prevalence among schoolchildren is 37.1%, and it can be caused by IDA, thalassemia, or celiac disease. Therefore, the target age for IDA among children is <2 years [2,3,4].

Causes of anemia due to iron can be either due to a decreased amount of available iron or increased iron needs. Decreased iron availability can be due to GIT factors like low nutritional iron, antiacids, celiac, Gastroesophageal reflux disease (GERD) and other factors, or it can be due to generalized diseases outside GIT like chronic inflammatory diseases, heart failure, chronic kidney diseases and obesity. However, causes of increased iron needs may happen in pregnancy, extreme exercise or blood loss from any organ. Figure 2 summarizes the causes of IDAs.

Figure-1: red blood cells formation and iron homeostasis [1]

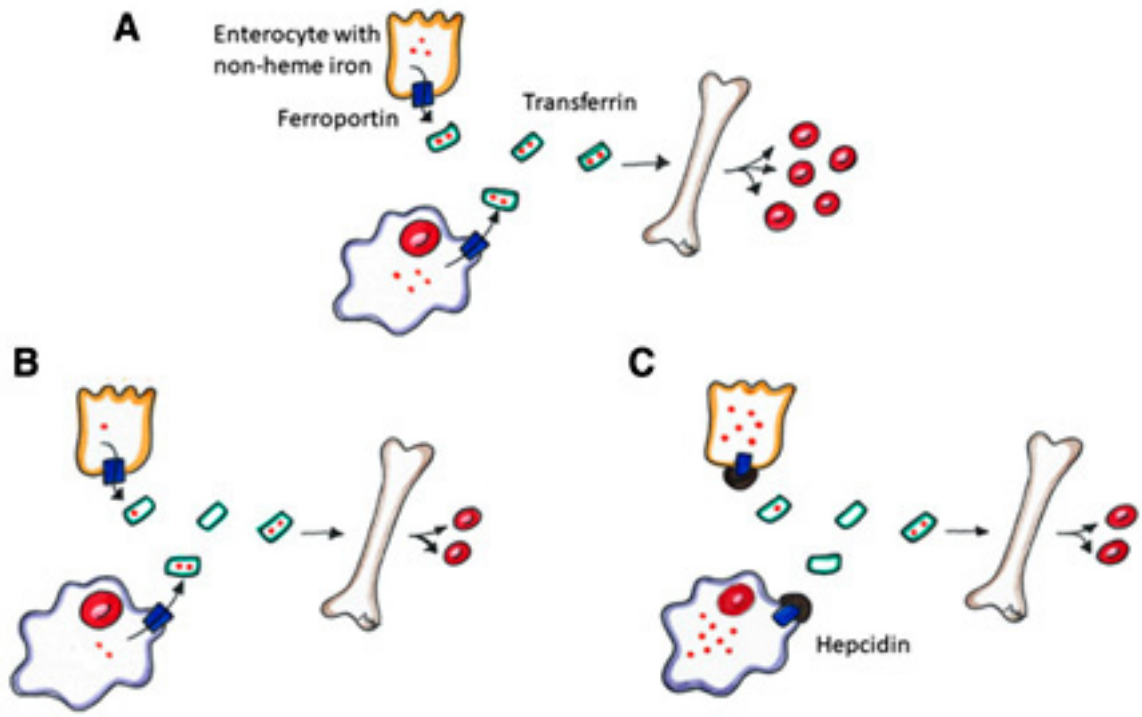
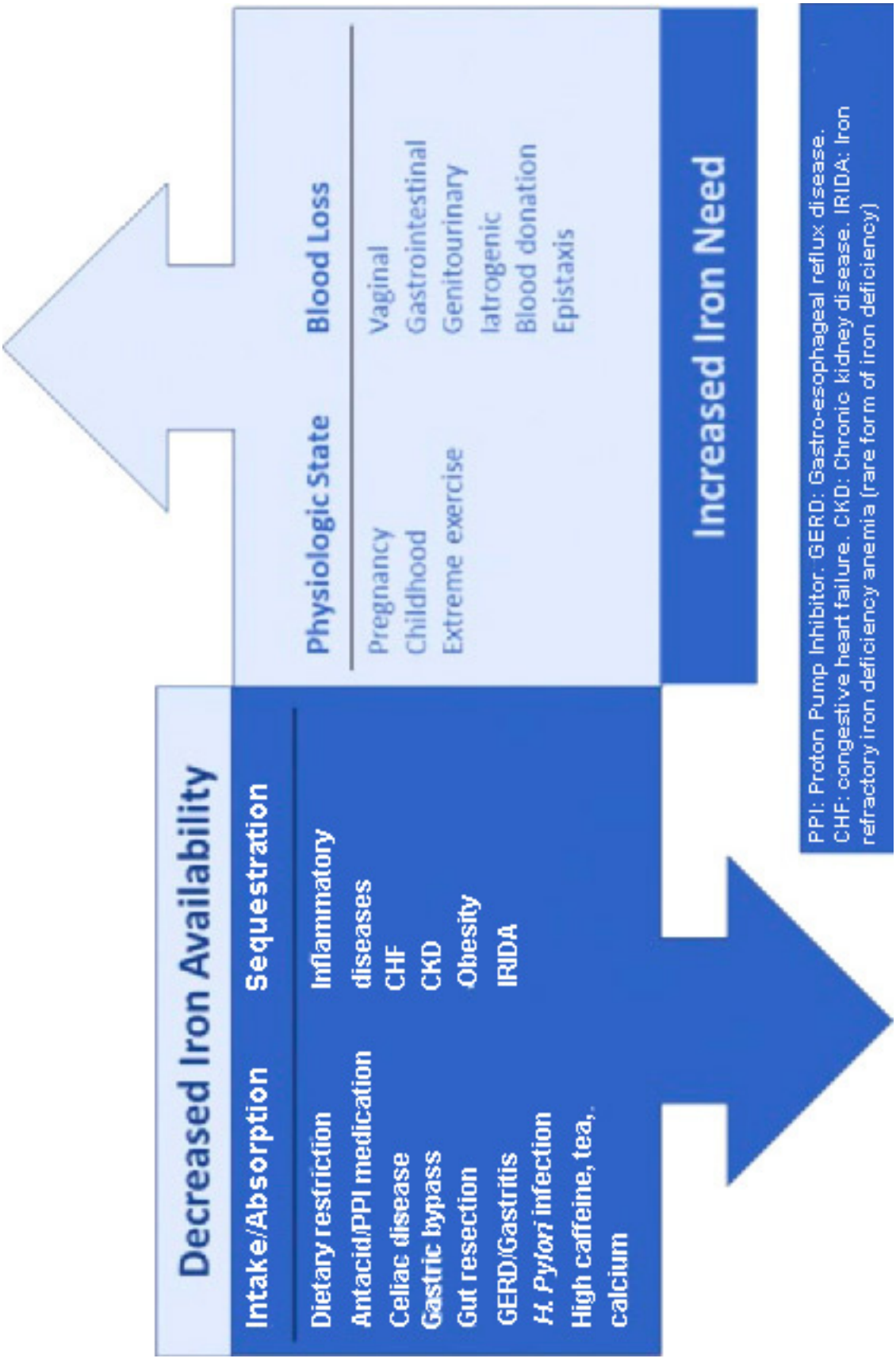


Figure 2: Causes of IDA in children [1]



The prevalence of IDA is significantly higher in developing countries than in rich countries. Mothers in poor countries are not educated enough about the importance of the early introduction of iron-fortified foods to their children. Unfortunately, they give low-iron foods for a long time until IDA occurs. Therefore, it is crucial to educate these mothers about the importance of early iron-fortified foods or administering oral iron drops, if necessary. Early introduction means starting iron sources in a child age below 2 years. Campaigns for health education can provide mass teaching to large numbers of mothers at the same time. Governments must support these campaigns through their Ministries of Health. Meanwhile, iron-fortified foods and oral iron supplements are readily available at markets and pharmacies [5,6].

Do we need to screen for IDA in each child or not? The answer is no. We do not need to screen each child except in certain situations. These situations include premature and low-birth-weight children and any child aged 6–24 months who is on a low-iron diet, especially in poor areas. Any child in a poor area should be screened for IDA routinely. Screening for IDA is a cheap, effective, and easy laboratory test. A complete blood count should be performed to measure blood hemoglobin level, reticulocyte count, and serum iron and ferritin levels. Any child discovered to have IDA must receive iron-fortified foods and oral iron supplements [7.8.9]. Figure 3 shows how to differentiate between the types of hypochromic anemias.

Figure 3: differential diagnosis of hypochromic anemias [10]

	Ferritin	Serum iron	TIBC	Transferrin saturation	Red cell distribution width	Marrow storage iron
Iron deficiency anemia	Low	Low	High	Low	High	Low
Thalassemias	Normal to high	Normal to high	Low to normal	Normal to high	Normal	Normal to high
Sideroblastic anemias	High	Normal to high	Low to normal	High	High	High
Anemia of chronic disease	Normal to high	Low	Low to normal	Low	Normal	Low to normal

Education about the correct weaning process is essential to prevent future IDA. Mothers should begin adding semisolid foods to breastfeeding milk at the age of 6 months. Semisolid foods provide iron to infants. It is crucial to educate mothers that breastfeeding alone is associated with low-iron levels. Another method is to start iron-fortified milk formulas at the age of 6 months of age. However, some mothers continue breastfeeding alone (exclusive breastfeeding) or start weaning with low-iron foods. Early diagnosis and treatment of IDA is important to protect infants from IDA disadvantages.

The main aim of this paper is to determine the impact of nutritional status of children in Jeddah city on the prevalence of IDA and to determine the bad habits of eating low iron foods and ignoring high iron foods. What is the impact of cow's milk on IDA? What is the effect of educational level of mothers on IDA? What will be the effect of early health education on the prevention of IDA in children?

In a large retrospective Saudi study on 498 children with IDA, results show that the largest prevalence was in infants. Early education and prevention is the major advice and regular monitoring is the key [11].

To our knowledge, this is the only study in Jeddah city which links the nutritional habits of children with different factors related to IDA. This link is crucial to direct health professionals to give more effort to early education of mothers on IDA parameters to prevent IDA in future. However, more studies are needed with larger samples and in multicentre to be more representative of Jeddah city.

Material and Methods

This study was conducted in a private clinic in Jeddah city. It was of one year duration between 2023 to 2024. Study model is cross sectional, and electronic questionnaires based which were used to evaluate the children's nutritional habits related to consumption of high iron foods. It was in Arabic language. Questions were divided into two areas: the first area asked about how much iron-rich foods children ate, and the second area asked about how many children ate harmful or low-iron foods. Sample size was 120 children (71 boys and 49 girls). All children with the diagnosis of IDA were included, while others were excluded. Electronic questionnaires were given to mothers of IDA children to fill out. Ethical approval was taken from the ethical committee in the clinic. Mothers were fully informed about what was needed and their written consent was taken.

Iron sources included animal, plant, grain, and legume sources, and iron-fortified foods. Generally, fast and harmful foods are low in iron. Figure-4 gives an idea about the amount of elemental iron in milligrams per certain foods. The highest sources are seafoods and meats. Other foods do contain iron in smaller amounts. This table must be given to mothers in primary care. Education about amounts of iron in foods is the simplest way to avoid IDA in future.

This questionnaire was electronically provided on Google Forms as a multiple-choice questionnaire and was given to mothers at each child visit in 2023. The questionnaire comprised five parts: small (0%–20%), few (20%–40%), middle (40%–60%), moderate (60%–80%), and huge (80%–100%). The data was documented in an Excel sheet. Regression analysis was the way used to analyze the data in SPSS software.

The first part of the questionnaire asked the mothers about the animal sources of iron:
(a) Determine the proportion of your child's intake of sea oysters or mussels.
(b) Determine the proportion of your child's intake of fish, salmon, or tuna.
(c) Determine the proportion of your child's intake of beef or chicken liver.
(d Determine the proportion of your child's intake of egg whites or yolks.
(e) Determine the percentage of your child's consumption of red meat.

The second part of the questionnaire asked the mothers about the vegetable sources of iron:
(a) Determine the proportion of your child's intake of spinach, kale, and beets.
(b) Determine the proportion of your child's intake of tomatoes or tomato paste.
(c) Determine the proportion of your child's intake of oyster or white mushrooms.

The third part of the questionnaire asked the mothers about the fruit sources of iron:
(a) Determine the proportion of your child's intake of peaches or peach juice.
(b) Determine the proportion of your child's intake of berries.
(c) Determine the proportion of your child's intake of watermelons.
(d) Determine the proportion of your child's intake of figs.
(e) Determine the proportion of your child's intake of bananas.
(f) Determine the proportion of your child's intake of apples.

The fourth part of the questionnaire asked the mothers about the cereal and legume sources of iron:
(a) Determine the proportion of your child's intake of chickpeas.
(b) Determine the proportion of your child's intake of white beans.
(c) Determine the proportion of your child's intake of pumpkin, sesame, and flax seeds.
(d) Determine the proportion of your child's intake of lentils.
(e) Determine the proportion of your child's intake of soybeans or its products, such as tofu.

The fifth part of the questionnaire asked mothers about low-iron foods or those that are harmful for children:
a) Determine the proportion of your child's intake of chips.
b) Determine the proportion of your child's consumption of fast food.
c) Determine the proportion of your child's consumption of canned juices.
d) Determine the proportion of your child's intake of sweets and candies.
e) Determine the proportion of your child's intake of colorful foods.
f) Determine the percentage of your child's intake of artificial cow's milk or its derivatives.

Figure 4 gives an idea about iron contents in certain foods. Figure-4 shows that the highest foods which contain iron are infant cereals followed by infant formulas. Both also contain other vitamins and minerals which are necessary for infants. It's good advice to give to mothers to use these two sources during infancy.

Figure 4: Amount of iron in foods sources [12]

4 - 5.9 months			6 - 8.9 months			9 - 11.9 months		
Food group	**% total iron intake**	**SE**	**Food group**	**% total iron intake**	**SE**	**Food group**	**% total iron intake**	**SE**
Infant formula	60.0	3.1	Infant cereal	47.9	3.0	Infant cereal	35.3	3.4
Infant cereal	36.4	3.2	Infant formula	41.9	2.6	Infant formula	33.7	2,4
Vitamin/mineral supplements	1.2	0.8	Vitamin/mineral supplements	1.4	0.8	Non-infant cereal	8.1	1.8
			Non-infant cereal	1.3	0.4	Vitamin/mineral supplements	4.7	2.1
			Crackers/ Pretzels/Rice cakes	1.2	0.3	Crackers/ Pretzels/Rice cakes	1.7	0.3
						Beef	1.7	1.1
						100% juice	1.2	0.2
						Pasta	1.0	0.3
						Baby Food dinners	1.0	0.2

Results

Table 1 shows that most animal sources of iron are not consumed by children with IDA, except eggs (white or yolk) and red meat, which are eaten in moderate quantities (60%–80%). If we add the numbers of (always plus sometimes) eaten eggs (white or yolk) and red meat, it will be 74.5% and 73.9%, respectively.

Fish, salmon, and tuna are consumed in middle quantities (40%–60%). If we add the numbers of (always and sometimes) consumed, it will be 54.2%.

Sea oysters or mussels and beef or chicken livers are not consumed by children with IDA. If we add (rare plus never) used for sea oysters or mussels and beef or chicken livers, it would be 95% and 81.3%, respectively. Both are used in small amounts (0%–20%): sea oysters and mussels (5%) and beef or chicken livers (18.7%).

This indicates that animal sources are not consumed in sufficient quantities by children with IDA, except eggs (white or yolk) and red meat, which are consumed in moderate quantities (60%–80%), followed by fish, salmon, and tuna, which are consumed in middle quantities (40%–60%).

Table 1: The percentage of the animal sources of iron that are consumed by children with IDA

	Always	Sometimes	Rarely	Never
Sea oysters or mussels	0	5.1%	15.3%	79.7%
Fish, salmon, or tuna	16.10%	38.1%	22.9%	22.9%
Beef or chicken liver	3.4%	15.3%	9.3%	72%
Egg whites or yolks	54.2%	20.3%	6.8%	18.6%
Red meat	34.7%	39%	11%	15.3%

Table 2 shows that most vegetable sources of iron are not consumed by children with IDA, except tomatoes, which are consumed in moderate quantities (60%–80%). If we add (always plus sometimes) tomatoes, the total will be 78.8%.

If we add (rare plus never) spinach, kale, and beets, it would make 79.9%. If we add (rare plus never used) mushrooms (oyster or white), the result will be 90.7%. Both are consumed in small or few negligible quantities; spinach, kale, and beets in few quantities (20.1%); and mushrooms (oyster or white) in small quantities (9.3%).

This indicates that children with IDA do not consume vegetable sources of iron in sufficient quantities, except tomatoes, which are consumed in moderate quantities (60%–80%).

Table 2: Percentage of vegetable sources of iron consumed by children with IDA

	Always	Sometimes	Rarely	Never
Spinach, kale, and beets	3.4%	16.9%	21.2%	58.5%
Tomatoes or tomato paste	53.4%	25.4%	11%	10.2%
Mushrooms (oyster or white)	3.4%	5.9%	11.9%	78.8%

Table 3 shows that most fruit sources of iron, except apple, watermelon, and banana, are not consumed by children with IDA. If we add (always and sometimes) apple, watermelon, and banana, the results will be 83.9%, 78%, and 72.9%, respectively.

Berries are consumed in middle quantities. If we add (always plus sometimes) berries, the total is 56%.

If we add (rare and never) figs and peaches, the results will be 79.6% and 72.9%, respectively. Figs and peaches are consumed at negligible quantities (20.4% and 27.1%, respectively).

This indicates that fruits are not consumed by children with IDA, except apple, watermelon, and banana, which are consumed in moderate quantities (60%–80%), followed by berries, which are consumed in middle quantities (40%–60%).

Table 3: Percentage of fruit sources of iron consumed by children with IDA

	Always	Sometimes	Rarely	Never
Peaches or peach juice	5.9%	21.2%	33.1%	39.8%
Berries	15.3%	40.7%	19.5%	24.5%
Watermelon	28%	50%	8.5%	13.6%
Figs	3.4%	16.9%	25.4%	54.2%
Banana	47.5%	25.4%	10.2%	16.9%
Apples	54.2%	29.7%	6.8%	9.3%

Table 4 shows that most cereal and legume sources of iron are not consumed by children with IDA, except lentils.

If we add (always plus sometimes) lentils and chickpeas, it will be 48.3% and 32.2%, respectively.

If we add (rare plus never) soybeans; white beans; pumpkin, sesame, and flax seeds; and chickpeas, it will be 80.5%, 78.8%, 75.4%, and 67.8%, respectively. These are consumed in small to few quantities (0%–40%): soybeans (19.5%); white beans (21.2%); and pumpkin, sesame, and flax seeds (24.6%).

This indicates that cereal and legume sources of iron are not consumed by children with IDA, except lentils, which are consumed in middle quantities (40%–60%), followed by chickpeas; white beans; and pumpkin, sesame, and flax seeds in few quantities (20%–40%).

Table 4: Percentage of cereal and legume sources of iron consumed by children with IDA

	Always	Sometimes	Rarely	Never
Chickpeas	9.3%	22.9%	21.2%	46.6%
White beans	2.5%	18.6%	18.6%	60.2%
Pumpkin, sesame, and flax seeds	10.2%	14.4%	17.8%	57.6%
Lentils	10.2%	38.1%	24.6%	27.1%
Soybeans or its products, such as tofu	7.6%	11.9%	13.6%	66.9%

Table 5 presents the consumption of low-quality foods by children with IDA. Low-quality foods are either low in iron or harmful to child's health. Unfortunately, low-quality foods are frequently consumed by children with IDA.

If we add (always plus sometimes) artificial cow's milk or its derivatives; chips; canned juices; sweets, candies, and fast food; and colorful foods, it will be 81.3%, 77.1%, 75.4%, 72%, and 50%, respectively.

This indicates that most low-quality foods, such as cow's milk and its derivatives, are consumed in large quantities (80%–100%), and chips, canned juices, sweets and candies, and fast foods, except colorful foods, are consumed in middle quantities (60%–80%).

Table 5: Percentage of children who consumed foods that do not contain iron or are harmful for children with IDA.

	Always	Sometimes	Rarely	Never
Chips	51.7%	25.4%	8.5%	14.4%
Fast food	32.2%	39.8%	11.9%	16.1%
Canned juices	55.9%	19.5%	10.2%	14.4%
Sweets and candies	48.3%	23.7%	15.3%	12.7%
Colorful foods	23.7%	26.3%	25.4%	24.6%
Artificial cow's milk or its derivatives	66.9%	14.4%	6.8%	11.9%

Table 6 presents a summary of foods consumed by children with IDA:
1–Most legume and vegetable sources are not consumed except for a few.
2–Animal sources, such as seafood and animal livers, are not consumed.
3–Most fruits are consumed in good quantities.
4–All low-quality foods are consumed in large quantities.
5–Cow's milk is the only food consumed in huge quantities.

Table 6: Summary of foods consumed by children with IDA.

Type of food	Small quantity 0%–20%	Few quantities 20%–40%	Middle quantities 40%–60%	Moderate quantities 60%–80%	Huge quantities 80%–100%
Animals	Sea oysters and mussels Beef and chicken livers		Fish, Salmon, and tuna	Eggs (white or yolk) and red meats	
Vegetables	Mushrooms (oyster or white)	Spinach, kale, and beets		Tomatoes	
Fruits		Peaches and figs	Berries	Apples, watermelon, and banana	
Legumes	Soybeans	Chickpeas; white beans; and pumpkin, sesame, and flax seeds	Lentils		
Low-quality foods			Colorful foods	Chips, canned juices, sweets, candies, and fast foods	Cow's milk and its derivatives

Figure 5: the needed amounts of elemental iron [18]

Age	*Iron supplementation or requirement*
Preterm (< 37 weeks' gestation) infants: 1 to 12 months	2 mg per kg per day supplementation if exclusively breastfed 1 mg per kg per day supplementation if using iron-fortified formula
Term infants: 4 to 6 months to 12 months	1 mg per kg per day supplementation if exclusively breastfed Supplementation not needed if using iron-fortified formula
Toddlers 1 to 3 years	Requires 7 mg per day; modify diet and/or supplement if anemic
Children 4 to 8 years	Requires 10 mg per day; modify diet and/or supplement if anemic

Discussion

Health professionals should be aware of the risk factors of IDA in children because early detection facilitates prevention. The risk factors associated with mothers are maternal age, low education level, and maternal anemia, particularly during pregnancy. The risk factors associated with children are premature age, child <2 years of age, child who consumes high quantities of cow's milk, infants who breastfeed exclusively, children with diarrhea or respiratory infections, obese children, and children on foods low in iron. Financial risk factors for IDA are also important because IDA is more common in poor areas with inadequate hygiene [13,14].

The primary risk factor of IDA among children in the future is excessive consumption of cow's milk or its derivatives. Therefore, history taking from mothers about the type of cow's milk consumed, its amount, and frequency is crucial to expect IDA. Additionally, it is very important to screen for IDA in a child who consumes excessive quantities of cow's milk. Furthermore, it is critical to give clear advice about the importance of breastfeeding, and if the child will consume cow's milk, it should be in small quantities. Cow's milk sources for children include milk, yogurt, butter, cheese, ice cream, and chocolate [15,16,17].

IDA can be easily prevented through maternal health education. Mass educational campaigns targeting mothers are effective. The most important clear and effective message to be given to mothers is the importance of the early introduction of iron-fortified foods to their children. This message is cheap and simple and can be easily applied in daily life. This simple step can decrease hospitalization and emergency visits due to IDA. Governments and ministries of health must support these campaigns because of their low cost and high yield, especially in poor areas. Figure-5 shows the amounts of elemental iron needed in infants, toddlers and children.

Infants who are breastfed exclusively without any other food are at risk of developing IDA at 9–12 months of age. The best approach is to start iron-fortified milk formula and foods early enough. To prevent IDA, mothers who exclusively breastfeed should start oral iron drops at 4 months of age. When mothers start weaning at 4–6 months, they should start iron-rich foods. Early initiation of iron-fortified milk or foods is the simplest, cheapest, and most effective step to prevent IDA. It is advisable to add vitamin C because it increases iron absorption. Vitamin C is found in strawberries, tomatoes, cantaloupes, and vegetables [19,20,21,22,23].

Dietary and therapeutic interventions are key steps in IDA management. The most important dietary intervention is iron-rich foods. However, oral iron drops are not needed in some cases. In mild cases of IDA, it is advisable to start intermittent oral iron drops, whereas continuous oral iron drops are recommended in moderate cases. Intravenous (IV) iron is needed in severe cases only. IV iron was administered under medical supervision in the day care department. If IDA does not respond to treatment, we must consider other causes of microcytic hypochromic anemia like β thalassemia trait, anemia of chronic disease, and celiac disease [24,25,26,27,28].

Changes in hematological parameters after iron administration to children must be monitored. The reticulocyte count is the first laboratory parameter to improve within several days after iron supplementation. However, hemoglobin levels take several weeks to improve. We must also monitor other related laboratory tests, including mean corpuscular volume, serum iron, and ferritin levels. Nevertheless, the most important parameter to be monitored is clinical improvement in symptoms after iron supplementation. History is an essential determinant of infant symptom improvement. Thus, mothers must visit clinics regularly with their infants [29,30].

IDA may disturb the neurological function of children if not treated and ignored for a long time. Chronic untreated IDA may affect growth; several papers say that untreated IDA may affect infant' neurological system development. In schoolchildren, IDA may affect a child's academic performance, concentration, and behavior. IDA can also affect child movement. Some studies advise health professionals to perform IDA laboratory tests on any child with autism or attention-deficit disorder because it may be caused by IDA. Thus it is crucial to treat IDA early enough to prevent possible neurological problems in children [31,32].

The relationship between IDA and Helicobacter pylori is controversial. Some studies say H. pylori has no role in IDA, whereas others have stated that it does. Studies claim there is a role report that H. pylori causes rapid iron uptake from the stomach. We do not know the specific reasons for this action by H. pylori. This possibility raises the point that we must always ask mothers whether their child has symptoms of gastroesophageal reflux disease. If these symptoms are present, it is important to perform H. pylori testing, including breath and stool tests. If H. pylori test results are positive, the condition must be treated early enough to prevent future IDA [33].

Conclusions: In Jeddah city, children with IDA do not eat iron-rich foods but consume huge quantities of low-quality foods. Most legume and vegetable sources of iron are not consumed, except a few (lentils and tomatoes). Many seafoods and animal livers are not consumed. All low-quality foods are consumed in large quantities. Cow's milk is the only type of food consumed in large quantities. The good news is that fruits are consumed in sufficient quantities. Foods high in iron that are consumed in moderate quantities include animals (eggs and red meats), vegetables (tomatoes), fruit (apples, watermelon, and banana). This indicates that IDA in children is mostly due to their dietary habits. Health education is the main solution. Mothers must be educated about the consumption of foods high in iron in children, consumption of iron-fortified foods or milk formulas in early infancy, regular clinic visits to check for IDA, avoiding exclusive breastfeeding, starting oral iron at 4–6 months of age, weaning foods high in iron, and consuming artificial cow's milk in small quantities only.

Acknowledgement
I offer my appreciation to the workers in Laluna private clinic in Jeddah city who helped me in distributing and collecting questionnaires and consents from mothers of IDA children.

Conflict of Interest Disclosure
I declare that there is no conflict of interest in this paper.

FUNDING
None.

ETHICS STATEMENT
Ethical approval was taken from the ethical committee in Laluna clinic in Jeddah city.

AVAILABILITY OF DATA
The data produced and/or analysed are accessible from the corresponding author upon sensible demand.

Informed Consent Statement
Mothers were fully informed, and their written consents were taken.

Authors' Contribution
I am a single author of this paper who fully supervised collecting data, then analyze it and write
up the manuscript.

References

[1] Shuoyan Ning and Michelle P. Zeller. Management of iron deficiency. Haematology. 2019.
PMID: 31622313. https://pubmed.ncbi.nlm.nih.gov/31622313/.
[2] Akodu OS, Disu EA, Njokanma OF, Kehinde OA. Iron deficiency anaemia among apparently healthy pre-school children in Lagos, Nigeria. Afr Health Sci. 2016 Mar;16(1):61-8. doi: 10.4314/ahs.v16i1.8. PMID: 27358614; PMCID: PMC4915399. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4915399/.
[3] Bortolini GA, Vitolo MR. Relationship between iron deficiency and anemia in children younger than 4 years. J Pediatr (Rio J). 2010 Nov-Dec;86(6):488-92. doi: 10.2223/JPED.2039. Epub 2010 Nov 17. PMID: 21085746. https://pubmed.ncbi.nlm.nih.gov/21085746/.
[4] Powers JM, Daniel CL, McCavit TL, Buchanan GR. Deficiencies in the Management of Iron Deficiency Anemia During Childhood. Pediatr Blood Cancer. 2016 Apr;63(4):743-5. doi: 10.1002/pbc.25861. Epub 2016 Jan 5. PMID: 26728130; PMCID: PMC4755821. https://pubmed.ncbi.nlm.nih.gov/26728130/.
[5] Al Ghwass MM, Halawa EF, Sabry SM, Ahmed D. Iron deficiency anemia in an Egyptian pediatric population: a cross-sectional study. Ann Afr Med. 2015 Jan-Mar;14(1):25-31. doi: 10.4103/1596-3519.148725. PMID: 25567692. https://pubmed.ncbi.nlm.nih.gov/25567692/.
[6] Lutter CK. Iron deficiency in young children in low-income countries and new approaches for its prevention. J Nutr. 2008 Dec;138(12):2523-8. doi: 10.3945/jn.108.095406. PMID: 19022983. https://pubmed.ncbi.nlm.nih.gov/19022983/.
[7] Jullien, S. Screening of iron deficiency anaemia in early childhood. BMC Pediatr 21 (Suppl 1), 337 (2021). https://doi.org/10.1186/s12887-021-02725-w.
[8] Siu AL; US Preventive Services Task Force. Screening for Iron Deficiency Anemia in Young Children: USPSTF Recommendation Statement. Pediatrics. 2015 Oct;136(4):746-52. doi: 10.1542/peds.2015-2567. Epub 2015 Sep 7. PMID: 26347426. https://pubmed.ncbi.nlm.nih.gov/26347426/.
[9] Mukhtarova N, Ha B, Diamond CA, Plumb AJ, Kling PJ. Serum Ferritin Threshold for Iron Deficiency Screening in One-Year-Old Children. J Pediatr. 2022 Jun;245:217-221. doi: 10.1016/j.jpeds.2022.01.050. Epub 2022 Jan 31. PMID: 35114287. https://pubmed.ncbi.nlm.nih.gov/35114287/.
[10] Patrick G. Gallagher. Anemia in the pediatric patient. PEDIATRIC HEMATOLOGY. 2022.
[11]Ahmed M Almutairi et al. A Multicenter Retrospective Chart Review Study Estimating the Prevalence of Iron Deficiency Anemia Among Infants, Toddlers, and Children in Riyadh, Saudi Arabia. Cureus. 2024.
[12] Kristen Finn, Cheryl Callen, Jatinder Bhatia, Kathleen Reidy, Lori J. Bechard, Ryan Carvalho.
Importance of Dietary Sources of Iron in Infants and Toddlers: Lessons from the FITS Study. Nutrients 2017
[13] André HP, Sperandio N, Siqueira RL, Franceschini SDCC, Priore SE. Food and nutrition insecurity indicators associated with iron deficiency anemia in Brazilian children: a systematic review. Cien Saude Colet. 2018 Apr;23(4):1159-1167. English, Portuguese. doi: 10.1590/1413-81232018234.16012016. PMID: 29694583. https://pubmed.ncbi.nlm.nih.gov/29694583/.
[14] Ji, S., Guan, X., Ma, L. et al. Iron deficiency anemia associated factors and early childhood caries in Qingdao. BMC Oral Health 22, 104 (2022). https://doi.org/10.1186/s12903-022-02127-z.
[15] Mukhtarova N, Ha B, Diamond CA, Plumb AJ, Kling PJ. Serum Ferritin Threshold for Iron Deficiency Screening in One-Year-Old Children. J Pediatr. 2022 Jun;245:217-221. doi: 10.1016/j.jpeds.2022.01.050. Epub 2022 Jan 31. PMID: 35114287. https://pubmed.ncbi.nlm.nih.gov/35114287/.
[16] López-Ruzafa E, Vázquez-López MA, Galera-Martínez R, Lendínez-Molinos F, Gómez-Bueno S, Martín-González M. Prevalence and associated factors of iron deficiency in Spanish children aged 1 to 11 years. Eur J Pediatr. 2021 Sep;180(9):2773-2780. doi: 10.1007/s00431-021-04037-8. Epub 2021 Mar 23. PMID: 33759019.
[17] Nowak S, Wang H, Schmidt B, Jarvinen KM. Vitamin D and iron status in children with food allergy. Ann Allergy Asthma Immunol. 2021 Jul;127(1):57-63. doi: 10.1016/j.anai.2021.02.027. Epub 2021 Mar 8. PMID: 33705915.
[18] MARY WANG. Iron Deficiency and Other Types of Anemia in Infants and Children. American Family Physician. 2016.
[19] Beinner MA, Lamounier JA. Recent experience with fortification of foods and beverages with iron for the control of iron-deficiency anemia in Brazilian children. Food Nutr Bull. 2003 Sep;24(3):268-74. doi: 10.1177/156482650302400304. PMID: 14564931.

[20] Beinner MA, Lamounier JA. Recent experience with fortification of foods and beverages with iron for the control of iron-deficiency anemia in Brazilian children. Food Nutr Bull. 2003 Sep;24(3):268-74. doi: 10.1177/156482650302400304. PMID: 14564931.
[21] Paulino CTDS, Nishijima M, Sarti FM. Association of Iron Supplementation Programs with Iron-Deficiency Anemia Outcomes among Children in Brazil. Nutrients. 2021 Apr 30;13(5):1524. doi: 10.3390/nu13051524. PMID: 33946398; PMCID: PMC8147124.
[22] Nwaba A, Su M, Rajamanickam V, Mezu-Nnabue K, Ubani U, Ikonne EU, Mezu-Ndubuisi O. Community Preventive Health Education Intervention for Pediatric Iron-Deficiency Anemia in Rural Southeast Nigeria. Ann Glob Health. 2022 Nov 21;88(1):105. doi: 10.5334/aogh.3625. PMID: 36474896; PMCID: PMC9695148.
[23] Prieto-Patron A, Detzel P, Ramayulis R, Sudikno, Irene, Wibowo Y. Impact of Fortified Infant Cereals on the Burden of Iron Deficiency Anemia in 6- to 23-Month-Old Indonesian Infants and Young Children: A Health Economic Simulation Model. Int J Environ Res Public Health. 2022 Apr 29;19(9):5416. doi: 10.3390/ijerph19095416. PMID: 35564811; PMCID: PMC9105951.
[24] Sun J, Zhang L, Cui J, Li S, Lu H, Zhang Y, Li H, Sun J, Baloch Z. Effect of dietary intervention treatment on children with iron deficiency anemia in China: a meta-analysis. Lipids Health Dis. 2018 May 10;17(1):108. doi: 10.1186/s12944-018-0749-x. PMID: 29747646; PMCID: PMC5944174.
[25] Li JY, Li L, Liu J, Liu XL, Liu JW. Efficacy of intermittent iron supplementation in children with mild iron-deficiency anemia. Zhongguo Dang Dai Er Ke Za Zhi. 2022 Feb 15;24(2):182-185. English, Chinese. doi: 10.7499/j.issn.1008-8830.2110036. PMID: 35209984; PMCID: PMC8884056.
[26] Aksan A, Zepp F, Anand S, Stein J. Intravenous ferric carboxymaltose for the management of iron deficiency and iron deficiency anaemia in children and adolescents: a review. Eur J Pediatr. 2022 Nov;181(11):3781-3793. doi: 10.1007/s00431-022-04582-w. Epub 2022 Sep 2. PMID: 36056175; PMCID: PMC9439269.
[27] Subramaniam G, Girish M. Iron deficiency anemia in children. Indian J Pediatr. 2015 Jun;82(6):558-64. doi: 10.1007/s12098-014-1643-9. Epub 2015 Feb 1. PMID: 25636824.
[28] Aydogan G, Keskin S, Akici F, Salcioglu Z, Bayram C, Uysalol EP, Gucer TNT, Ersoy G, Ozdemir N. Causes of Hypochromic Microcytic Anemia in Children and Evaluation of Laboratory Parameters in the Differentiation. J Pediatr Hematol Oncol. 2019 May;41(4):e221-e223. doi: 10.1097/MPH.0000000000001382. PMID: 30557168.
[29] Russo G, Guardabasso V, Romano F, Corti P, Samperi P, Condorelli A, Sainati L, Maruzzi M, Facchini E, Fasoli S, Giona F, Caselli D, Pizzato C, Marinoni M, Boscarol G, Bertoni E, Casciana ML, Tucci F, Capolsini I, Notarangelo LD, Giordano P, Ramenghi U, Colombatti R. Monitoring oral iron therapy in children with iron deficiency anemia: an observational, prospective, multicenter study of AIEOP patients (Associazione Italiana Emato-Oncologia Pediatrica). Ann Hematol. 2020 Mar;99(3):413-420. doi: 10.1007/s00277-020-03906-w. Epub 2020 Jan 21. PMID: 31965272.
[30] Zheng J, Liu J, Yang W. Association of Iron-Deficiency Anemia and Non-Iron-Deficiency Anemia with Neurobehavioral Development in Children Aged 6-24 Months. Nutrients. 2021 Sep 28;13(10):3423. doi: 10.3390/nu13103423. PMID: 34684422; PMCID: PMC8537382.
[31] Pivina L, Semenova Y, Doşa MD, Dauletyarova M, Bjørklund G. Iron Deficiency, Cognitive Functions, and Neurobehavioral Disorders in Children. J Mol Neurosci. 2019 May;68(1):1-10. doi: 10.1007/s12031-019-01276-1. Epub 2019 Feb 18. PMID: 30778834.
[32] Zahmatkeshan, M., Karimi, M., Geramizadeh, B. et al. Association between Helicobacter pylori Infection and Iron Deficiency Anemia in School-aged Iranian Children. Indian Pediatr 56, 387–389 (2019). https://doi.org/10.1007/s13312-019-1536-0
[33] Konno M. [Iron-deficiency anemia in children]. Nihon Rinsho. 2009 Dec;67(12):2345-51. Japanese. PMID: 19999123. https://pubmed.ncbi.nlm.nih.gov/19999123/.

Challenges Saudi Patients Face with Antihypertensive Medications: The Role of Pharmacy Services in Enhancing Awareness and Medication Management

Abdulmohsen Saad Y Al Ahmari

Pharmacy intern at King Khalid University, Abha, Saudi Arabia

Received: April 2025. Accepted: May 2025; Published:June 1, 2025.
Citation: Abdulmohsen Saad Y AlAhmari. Challenges Saudi Patients Face with Antihypertensive Medications: The Role of Pharmacy Services in Enhancing Awareness and Medication Management. World Family Medicine. June 2025; 23(4): 26 - 39.
DOI: 10.5742/MEWFM.2025.795257868

Abstract

Background: Hypertension remains a leading public health concern in Saudi Arabia, with many patients experiencing challenges in medication adherence, awareness, and blood pressure control. Pharmacists have the potential to play a vital role in improving these outcomes through education and ongoing support.

Objective: To assess awareness, medication management practices, and the utilization of pharmacy services among hypertensive patients attending primary healthcare centers (PHCs) in Saudi Arabia.

Methods: A descriptive cross-sectional study was conducted among 235 adult Saudi hypertensive patients attending urban and rural PHCs in the Abha region. Data were collected using a structured, self-administered questionnaire developed based on literature and expert input. The questionnaire assessed sociodemographic characteristics, medication adherence, awareness of antihypertensive medications, use of pharmacy services, and self-reported blood pressure control. Data analysis was performed using SPSS version 18. Awareness scores were categorized as poor (<60%) or good (>60%), and associations were tested using the Chi-square test, with a significance threshold set at $p < 0.05$.

Results: The majority of participants (76.6%) demonstrated poor awareness of their antihypertensive medications, while only 23.4% had good awareness. Additionally, 56.2% of patients reported never receiving medication information from a pharmacist. Only 21.3% of patients reported feeling very clear about the purpose of their medications, and 26.4% had received pharmacist-led education on lifestyle modifications. Key factors significantly associated with better awareness included gender ($p = .039$), marital status ($p = .006$), education level ($p = .032$), duration of hypertension ($p = .004$), and frequency of blood pressure monitoring ($p = .049$).

Conclusion: There is an urgent need to improve hypertension management in primary care by enhancing patient education, addressing barriers to adherence, and expanding the role of pharmacists in chronic disease support.

Keywords:
Hypertension management, patient awareness, medication adherence, pharmacy services, primary healthcare, Saudi Arabia.

Introduction

Globally, hypertension is an increasing public health issue and particularly in Saudi Arabia where lifestyle changes and urbanization have contributed to its rising prevalence (1,2). Despite the availability of effective antihypertensive medications, suboptimal blood pressure control remains a significant issue among patients (3). This problem is often compounded by challenges related to medication adherence, awareness, and patient-pharmacy interactions.

Generally, hypertension, frequently termed high blood pressure, poses a substantial public health challenge (4). It stands as a key risk factor for the development of cardiovascular diseases, cerebrovascular accidents (stroke), and chronic renal disease (5). Recent data indicate a rising prevalence of hypertension within the adult population of Saudi Arabia, attributable in part to the aging demographic, sedentary behaviors, suboptimal dietary patterns, obesity, and other non-communicable disease risk factors (6, 7).

The cornerstone of hypertension management is long-term adherence to antihypertensive medications, along with lifestyle modifications such as reducing salt intake, increasing physical activity, and managing stress (8). Despite the availability of effective medications, a significant proportion of patients struggle to maintain optimal blood pressure control. Poor adherence to prescribed antihypertensive regimens is a key contributor to treatment failure and complications (9). Common challenges faced by patients include forgetfulness, medication side effects, complex regimens, lack of understanding about the importance of adherence, financial constraints, and limited access to ongoing education and counseling (10).

Pharmacy services, especially within the primary health care system, are in a unique position to support hypertensive patients in overcoming these barriers. Pharmacists can play a vital role in patient education, counseling, identifying medication-related problems, improving medication adherence, and providing follow-up care (11). In Saudi Arabia, where Primary Health Care Centers (PHCCs) serve as the first point of contact for many patients, integrating pharmacist-led interventions could significantly improve hypertension outcomes. This study aims to investigate the challenges Saudi patients face with their antihypertensive medications and explore the current and potential roles of pharmacy services in enhancing patients' awareness, medication management, and blood pressure control. Understanding these factors can contribute to improving the quality of care delivered in PHCCs and inform future strategies to strengthen the role of pharmacists in chronic disease management.

Methodology

A descriptive cross-sectional study was conducted using a structured questionnaire to gather data on the awareness, medication management practices, and utilization of pharmacy services among hypertensive patients attending primary healthcare centers in both urban and rural settings in Saudi Arabia. The study population consisted of adult Saudi patients diagnosed with hypertension who were attending primary healthcare centers in the Abha region. A convenience sample of 235 patients was simulated for this pilot study. Participants were selected using purposive sampling, ensuring variety in terms of healthcare settings and patient experiences with hypertension management. Data collection was carried out using a structured, self-administered questionnaire developed specifically for the study. The questionnaire, which was designed based on relevant literature and expert input, aimed to capture sociodemographic details, medication adherence practices, patient awareness and education about antihypertensive medications, and utilization of pharmacy services. Additionally, it included questions on self-reported blood pressure control. The questionnaire combined closed-ended and multiple-response questions to facilitate detailed data collection while maintaining manageability. A pre-test of the tool was conducted using 15 simulated responses to ensure its clarity, consistency, and relevance to the study objectives. Data were collected at selected primary healthcare centers across urban and rural areas. Eligible participants—adult Saudi patients diagnosed with hypertension—were approached in the waiting areas of the centers and invited to participate voluntarily. A trained data collector or healthcare professional was available on-site to assist participants, particularly those who were illiterate, to ensure inclusivity. All responses were collected anonymously, and the data were entered into a secured Excel database for analysis.

Data analysis

Data analysis was conducted using SPSS version 18 (SPSS Inc., Chicago, IL, USA). The awareness score was derived by assigning one point to each correct response on a structured questionnaire. Patients with an overall awareness score below 60% were classified as having poor awareness, while those scoring above 60% were categorized as having good awareness. Descriptive analysis using frequency and % were used to assess sample characteristics, awareness and blood pressure control measures. All graphs were initiated using Microsoft Excel Software. All relations were done using cross-tabulation using Pearson X2 test and exact probability test for small frequency distributions. P value less than 0.05 was considered for statistical significance.

Results

Table 1 presents the socio-demographic characteristics of 235 hypertensive patients attending Primary Health Care Centers (PHCs) in Saudi Arabia. The most represented age group was 41–50 years (78; 33.2%), followed by those aged 31–40 (52; 22.1%) and 18–30 (39; 16.6%), while older age groups, including 51–60 (35; 14.9%) and 61 and above (31; 13.2%), were less represented. Males constituted a higher proportion of the sample (134; 57.0%) compared to females (101; 43.0%). As for marital status, the majority were married (96; 40.9%), while 90 (38.3%) were divorced or widowed, and 49 (20.9%) were single. Educational level varied, with the largest group holding undergraduate degrees (78; 33.2%), followed by those with secondary (53; 22.6%) and postgraduate (43; 18.3%) education; a smaller number had only primary education (38; 16.2%) or no formal education (23; 9.8%). Regarding the duration of hypertension, 72 patients (30.6%) had been diagnosed for 1–3 years, 67 (28.5%) for more than 6 years, and 52 (22.1%) for 4–6 years, while 23 (9.8%) and 21 (8.9%) were recorded as having hypertension for "<1 year" and "less than 1 year," respectively. Most patients reported attending urban PHCs (150; 63.8%), while 85 (36.2%) visited rural centers.

Table 1. Socio-demographic characteristics of the study hypertensive patients attending PHCs in Saudi Arabia (N=235)

Demographic data	No	%
Age in years		
18-30	39	16.6%
31-40	52	22.1%
41-50	78	33.2%
51-60	35	14.9%
61 and above	31	13.2%
Gender		
Male	134	57.0%
Female	101	43.0%
Marital status		
Single	49	20.9%
Married	96	40.9%
Divorced / widow	90	38.3%
Educational level		
No formal education	23	9.8%
Primary school	38	16.2%
Secondary school	53	22.6%
Undergraduate degree	78	33.2%
Postgraduate degree	43	18.3%
Duration of hypertension		
<1 year	23	9.8%
1-3 years	72	30.6%
4-6 years	52	22.1%
Less than 1 year	21	8.9%
More than 6 years	67	28.5%
Primary Health Care Center, do you visit		
Rural area	85	36.2%
Urban area	150	63.8%

Table 2 outlines the medication management practices among hypertensive patients attending PHCs in Saudi Arabia. A significant proportion of patients were prescribed a single antihypertensive medication (81; 34.5%), followed by those taking three medications (57; 24.3%) and two medications (55; 23.4%), while 42 patients (17.9%) were on more than three medications. When asked about adherence, only 62 (26.4%) reported it was easy to take their medications as prescribed, whereas more than half (127; 54.0%) found it manageable only sometimes, and 46 (19.6%) admitted difficulty. The most common challenge cited was conflicts with travel or work schedules (95; 40.4%), followed by issues such as difficulty remembering dosages (63; 26.8%), lack of motivation or forgetfulness (58; 24.7%), and simply forgetting to take the medication (56; 23.8%). Other notable barriers included medication side effects and cost (both 53; 22.6%), difficulty swallowing pills (50; 21.3%), lack of understanding about medications (49; 20.9%), psychological barriers (47; 20.0%), and complex schedules (37; 15.7%). To improve adherence, patients reported that daily pillboxes and written instructions with clear schedules (both 51; 21.7%) were the most helpful reminders, followed by in-person or phone reminders from healthcare professionals (47; 20.0%) and mobile app notifications (42; 17.9%).

Table 2. Medication Management Practices, Challenges, and Support among Hypertensive Patients Attending PHCs in Saudi Arabia (N=235)

Medication Management	No	%
Number of antihypertensive medications are you currently prescribed		
1 medication	81	34.5%
2 medications	55	23.4%
3 medications	57	24.3%
More than 3 medications	42	17.9%
You find it easy to take your antihypertensive medications as prescribed		
Yes	62	26.4%
Sometimes	127	54.0%
No	46	19.6%
What challenges do you face in taking your medications		
Travel/work schedule conflicts	95	40.4%
Difficulty remembering the dosage	63	26.8%
Lack of motivation or forgetfulness	58	24.7%
Forgetting to take the medication	56	23.8%
Side effects of the medication	53	22.6%
Cost of medications	53	22.6%
Difficulty with swallowing pills	50	21.3%
Lack of understanding about the medication	49	20.9%
Emotional or psychological barriers	47	20.0%
Complex medication schedule	37	15.7%
Type of reminder or assistance help you take your medications regularly		
Daily pillboxes	51	21.7%
Written instructions with clear schedules	51	21.7%
In-person reminders or phone calls from healthcare professionals	47	20.0%
Mobile apps/reminder notifications	42	17.9%
Pharmacy calls	27	11.5%
Weekly follow-up calls from the pharmacy	17	7.2%

Table 3 highlights the level of awareness and educational needs regarding antihypertensive medications among 235 patients attending PHCs in Saudi Arabia. Less than half of the participants (103; 43.8%) reported receiving information about their medications from a pharmacist, while the majority (132; 56.2%) did not. When asked about their understanding of the purpose and benefits of their medications, only 50 participants (21.3%) felt very clear, whereas most were either somewhat clear (110; 46.8%) or not clear at all (75; 31.9%). Understanding of how antihypertensive medications help control blood pressure was similarly limited, with only 88 (37.4%) responding affirmatively, while 81 (34.5%) were unsure and 66 (28.1%) lacked understanding. Patients expressed interest in additional information, particularly regarding when to seek medical help for side effects (95; 40.4%), possible side effects (91; 38.7%), the importance of adherence (89; 37.9%), and how medications work (86; 36.6%). Only 62 participants (26.4%) had received pharmacist education on lifestyle changes, while the majority either had not (119; 50.6%) or were unsure (54; 23.0%).

Table 3: Awareness and Educational Needs Regarding Antihypertensive Medications Among Patients Attending PHCs in Saudi Arabia (N=235)

Awareness	No	%
Received information about your antihypertensive medications from your pharmacist		
Yes	103	43.8%
No	132	56.2%
How clear are you about the purpose and benefits of the antihypertensive medication(s) you take?		
Not clear at all	75	31.9%
Somewhat clear	110	46.8%
Very clear	50	21.3%
Do you understand how antihypertensive medications can help in controlling blood pressure?		
Yes	88	37.4%
No	66	28.1%
Not sure	81	34.5%
What additional information would help you better understand your antihypertensive medications?		
When to seek medical help for side effects	95	40.4%
Possible side effects	91	38.7%
The importance of regular use and adherence	89	37.9%
How the medication works to lower blood pressure	86	36.6%
Information on the impact of lifestyle changes	81	34.5%
Others	32	13.6%
Have you ever been educated by a pharmacist regarding lifestyle changes that can help control blood pressure?		
Yes	62	26.4%
No	119	50.6%
Not sure	54	23.0%

Figure 1 shows the overall level of knowledge and awareness about antihypertensive medications among hypertensive patients attending PHCs in Saudi Arabia (N=235). The majority of participants (180; 76.6%) had a poor level of awareness, while only 55 individuals (23.4%) showed a good knowledge and awareness of their antihypertensive treatment.

Figure 1. The Overall Hypertension Patients' Knowledge and Awareness about Antihypertensive Medications (N=235)

Table 4 presents data on the utilization of pharmacy services and patient preferences for support in managing hypertension. Only a minority of participants reported frequent pharmacist visits for advice related to antihypertensive medications (43; 18.3%), while most interacted occasionally (69; 29.4%), rarely (67; 28.5%), or never (56; 23.8%). When asked whether pharmacy services such as counseling, medication reviews, or follow-up had helped manage their blood pressure, responses were mixed: 84 (35.7%) agreed, 81 (34.5%) disagreed, and 70 (29.8%) were unsure. Considering additional services desired, patients expressed strong interest in understanding side effects (84; 35.7%), regular medication reviews (83; 35.3%), and medication reminders (78; 33.2%). Other requested supports included lifestyle education (70; 29.8%), blood pressure monitoring (69; 29.4%), and assistance with medication costs (65; 27.7%). Regarding preferred methods for receiving education and support, group sessions (56; 23.8%) and digital resources (44; 18.7%) were favored, while fewer patients preferred direct phone or text follow-ups (41; 17.4%), printed materials (40; 17.0%), or one-on-one counseling (32; 13.6% in general and 22; 9.4% during pharmacy visits).

Table 4: Utilization of Pharmacy Services and Patient Preferences for Hypertension Management Support in Saudi Arabia (N=235)

Services	No	%
How often do you visit a pharmacist for advice or support related to your antihypertensive medications?		
Frequently (at every visit)	43	18.3%
Occasionally (few times per year)	69	29.4%
Rarely	67	28.5%
Never	56	23.8%
Do you feel that pharmacy services (such as counseling, medication reviews, follow-up) have helped you manage your blood pressure better?		
Yes	84	35.7%
No	81	34.5%
Not sure	70	29.8%
What additional services would you like from pharmacists to help you better manage your hypertension?		
Side effects understandings	84	35.7%
Regular medication reviews	83	35.3%
Reminders for medication intake	78	33.2%
Lifestyle education	70	29.8%
BP monitoring	69	29.4%
Help with managing the cost of medications	65	27.7%
How would you prefer to receive education and support from your pharmacist?		
Group educational sessions	56	23.8%
Online or mobile app resources	44	18.7%
Phone calls or text messages for FU	41	17.4%
Written pamphlets and leaflets	40	17.0%
1-on-1 counseling	32	13.6%
One-on-one counseling during pharmacy visit	22	9.4%

Table 5 clarifies data on blood pressure monitoring habits, control status, and perceived barriers among hypertensive patients. Only about one-third of the participants (77; 32.8%) reported checking their blood pressure at every healthcare visit, while others did so occasionally (66; 28.1%) or rarely (71; 30.2%), and a small group (21; 8.9%) never monitored it. When asked if they had achieved their target blood pressure, 81 (34.5%) responded positively, 78 (33.2%) had not, and 76 (32.3%) were unsure. Key barriers to better control included lack of follow-up or support from healthcare providers (97; 41.3%) and side effects from medication (78; 33.2%), followed by limited understanding of blood pressure management (66; 28.1%), stress or mental health issues (64; 27.2%), poor adherence (60; 25.5%), and financial challenges (56; 23.8%). Exactly 93 patients (39.6%) believed that better education and support from pharmacists could help improve their blood pressure control.

Table 5. Blood Pressure Monitoring, Control Status, and Perceived Barriers among Hypertensive Patients Attending PHCs in Saudi Arabia (N=235)

Blood Pressure Control	No	%
How often do you check your blood pressure?		
At every healthcare visit	77	32.8%
Occasionally (e.g., once a month)	66	28.1%
Rarely	71	30.2%
Never	21	8.9%
Have you achieved your target blood pressure goal, as advised by your healthcare provider?		
Yes	81	34.5%
No	78	33.2%
Not sure	76	32.3%
Barriers you feel prevent you from achieving better blood pressure control		
Lack of follow-up or support from healthcare providers	97	41.3%
Side effects of medication	78	33.2%
Lack of understanding about the importance of controlling blood pressure	66	28.1%
Stress or mental health issues	64	27.2%
Lack of medication adherence	60	25.5%
Financial challenges	56	23.8%
Others	33	14.0%
Do you think better education and support from pharmacists could help you achieve better blood pressure control?		
Yes	93	39.6%
No	71	30.2%
Not sure	71	30.2%

Figure 2 illustrates the suggestions provided by hypertensive patients for improving pharmacy services to better support their condition. The most frequently recommended improvements included providing more educational materials and resources (91; 38.7%) and enhancing accessibility of pharmacy services, such as extended hours or home delivery (91; 38.7%). Additionally, a significant number of participants (87; 37.0%) reported the need for further training of pharmacists to better support hypertensive patients. Personalized follow-up was also suggested by 70 individuals (29.8%).

Figure 2. The Suggestions Provided by The Study Patients for Improving Pharmacy Services to Better Support Patients with Hypertension

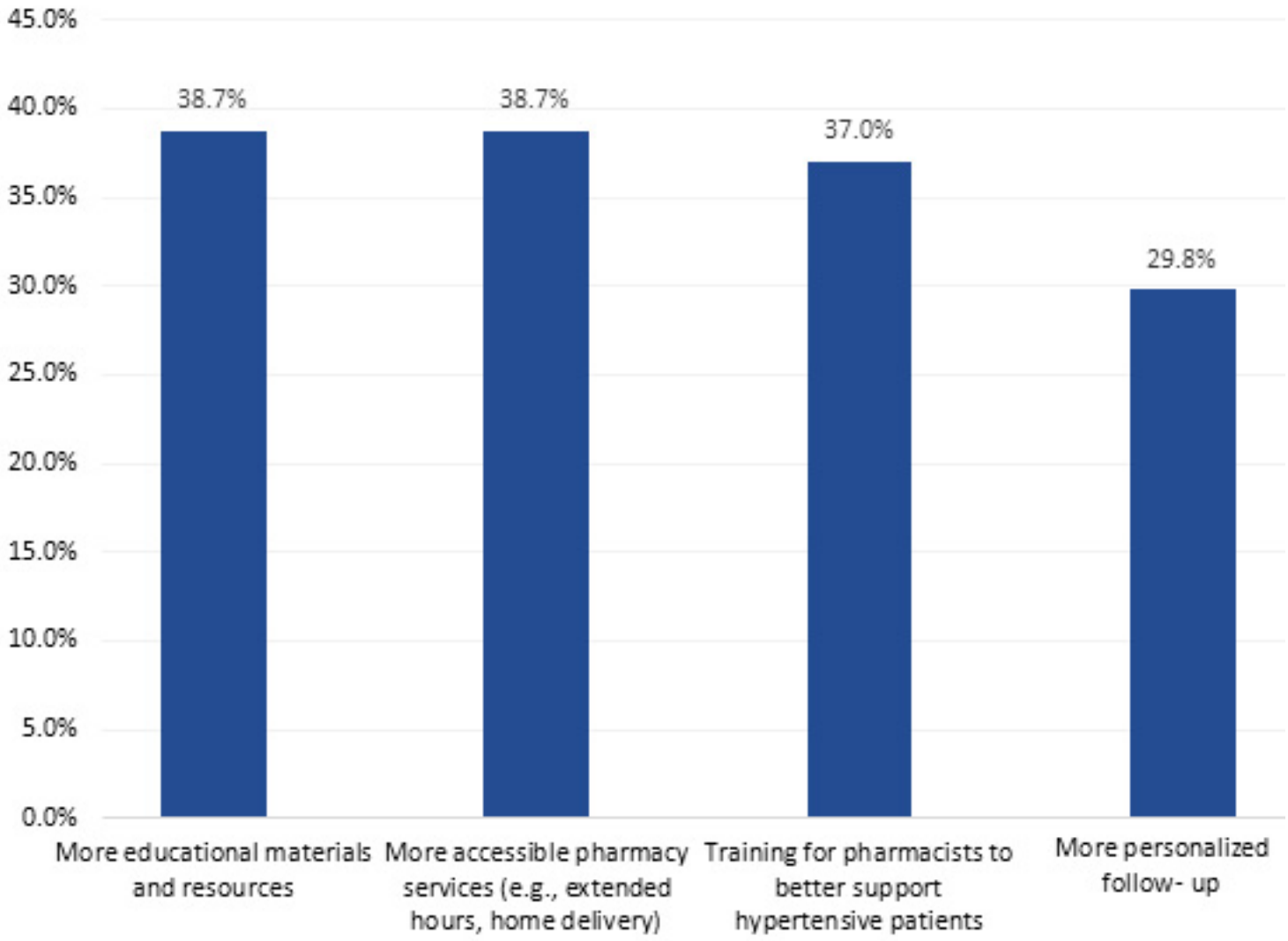


Table 6 highlights the factors significantly associated with patients' overall awareness of antihypertensive medications. Gender was a significant factor (p = .039), with a higher proportion of males (28.4%) having good awareness compared to females (16.8%). Marital status also showed a significant association (p = .006), where married patients had the highest level of good awareness (31.3%), followed by single individuals (28.6%), while divorced or widowed participants had the lowest (12.2%). Educational level was another key factor (p = .032), with those holding an undergraduate degree showing the highest awareness (33.3%), compared to only 9.3% among those with postgraduate degrees and 17.0% among secondary school graduates. Duration of hypertension was significantly related to awareness (p = .004), as patients with shorter durations of hypertension (e.g., <1 year: 34.8%; 1–3 years: 34.7%) had better awareness than those with longer durations (e.g., more than 6 years: 20.9%; 4–6 years: 15.4%).

Table 6. Factors Associated with Overall Awareness Level About Antihypertensive Medications Among Hypertensive Patients (N=235)

Factors		Overall awareness level				p-value
		Poor		Good		
		No	%	No	%	
Age in years	18-30	32	82.1%	7	17.9%	.260
	31-40	35	67.3%	17	32.7%	
	41-50	58	74.4%	20	25.6%	
	51-60	30	85.7%	5	14.3%	
	61 and above	25	80.6%	6	19.4%	
Gender	Male	96	71.6%	38	28.4%	.039*
	Female	84	83.2%	17	16.8%	
Marital status	Single	35	71.4%	14	28.6%	.006*
	Married	66	68.8%	30	31.3%	
	Divorced / widow	79	87.8%	11	12.2%	
Educational level	No formal education	17	73.9%	6	26.1%	.032*
	Primary school	28	73.7%	10	26.3%	
	Secondary school	44	83.0%	9	17.0%	
	Undergraduate degree	52	66.7%	26	33.3%	
	Postgraduate degree	39	90.7%	4	9.3%	
Duration of hypertension	<1 year	15	65.2%	8	34.8%	.004*^
	1-3 years	47	65.3%	25	34.7%	
	4-6 years	44	84.6%	8	15.4%	
	Less than 1 year	21	100.0%	0	0.0%	
	More than 6 years	53	79.1%	14	20.9%	
Primary Health Care Center do you visit	Rural area	69	81.2%	16	18.8%	.212
	Urban area	111	74.0%	39	26.0%	
Number of antihypertensive medications are you currently prescribed	1 medication	57	70.4%	24	29.6%	.232
	2 medications	47	85.5%	8	14.5%	
	3 medications	43	75.4%	14	24.6%	
	More than 3 medications	33	78.6%	9	21.4%	
You find it easy to take your antihypertensive medications as prescribed	Yes	50	80.6%	12	19.4%	.395
	Sometimes	98	77.2%	29	22.8%	
	No	32	69.6%	14	30.4%	
Type of reminder or assistance help you take your medications regularly	Daily pillboxes	37	72.5%	14	27.5%	.969^
	In-person reminders or phone calls from healthcare professionals	36	76.6%	11	23.4%	
	Mobile apps/reminder notifications	33	78.6%	9	21.4%	
	Pharmacy calls	22	81.5%	5	18.5%	
	Weekly follow-up calls from the pharmacy	13	76.5%	4	23.5%	
	Written instructions with clear schedules	39	76.5%	12	23.5%	

P: Pearson X2 test ^: Exact probability test * P < 0.05 (significant)

Table 7 examines the association between blood pressure monitoring and control with overall awareness levels regarding antihypertensive medications. Among the variables assessed, the frequency of blood pressure monitoring showed a statistically significant association with awareness levels (p = .049). Notably, a higher percentage of patients with poor awareness reported checking their blood pressure at every healthcare visit (36.1%) or occasionally (29.4%), while those with good awareness were more likely to monitor their blood pressure rarely (43.6%).

Table 7. Association Between Blood Pressure Monitoring and Control with Overall Awareness Level About Antihypertensive Medications Among Hypertensive Patients (N=235)

BP control	Overall awareness level				p-value
	Poor		Good		
	No	%	No	%	
How often do you visit a pharmacist for advice or support related to your antihypertensive medications?					
Frequently (at every visit)	31	17.2%	12	21.8%	.816
Occasionally (few times per year)	53	29.4%	16	29.1%	
Rarely	51	28.3%	16	29.1%	
Never	45	25.0%	11	20.0%	
How would you prefer to receive education and support from your pharmacist?					
1-on-1 counseling	24	13.3%	8	14.5%	.499^
Group educational sessions	45	25.0%	11	20.0%	
One-on-one counseling during pharmacy visit	20	11.1%	2	3.6%	
Online or mobile app resources	32	17.8%	12	21.8%	
Phone calls or text messages for FU	31	17.2%	10	18.2%	
Written pamphlets and leaflets	28	15.6%	12	21.8%	
How often do you check your blood pressure?					
At every healthcare visit	65	36.1%	12	21.8%	.049*
Occasionally (e.g., once a month)	53	29.4%	13	23.6%	
Rarely	47	26.1%	24	43.6%	
Never	15	8.3%	6	10.9%	
Have you achieved your target blood pressure goal, as advised by your healthcare provider?					.435
Yes	61	33.9%	20	36.4%	
No	57	31.7%	21	38.2%	
Not sure	62	34.4%	14	25.5%	

P: Pearson X2 test ^: Exact probability test * P < 0.05 (significant)

Discussion

The current study focused on hypertensive patients in Saudi Arabia and how they manage their medications. The fact that most participants were middle-aged (41–50 years) simulates global patterns where high blood pressure becomes more common with age, though it's increasingly seen in younger people due to lifestyle choices (12). Interestingly, there were more male participants than female, which differs from some studies elsewhere and might point to cultural differences in how men and women seek healthcare (13). The majority of patients were married and a good number of patients had higher education. In regard to taking medications, it was a big challenge for most patients, which is similar to what other studies in the Middle East have found, with things like forgetting doses, complicated schedules, and side effects being common hurdles (14). Many patients were on several blood pressure medications, which follows international guidelines, but this also made it harder for them to keep up with their treatment. This highlights the need to simplify medication plans whenever possible (15). The most common reasons for missing medications were travel and work, which is consistent with research in other busy urban areas where job demands get in the way of medication routines (16). On a positive note, things like pillboxes and written instructions were helpful for remembering medications, which backs up previous research. However, technology like mobile apps wasn't used as much, signifying there's room to incorporate more digital health tools (17).

In regard to patient's awareness, our study revealed a significant defect in awareness and understanding of antihypertensive medications among hypertensive patients in Saudi Arabia. A concerning proportion of patients did not receive medication information from pharmacists, and only a small percentage felt very clear about the purpose and benefits of their treatment. This matches with previous studies in the region, where poor patient education has been linked to lower adherence and poorer blood pressure control (18-20). The limited understanding of how antihypertensive medications work is particularly troubling, as patients who do not grasp the long-term benefits of their treatment may be less motivated to adhere to therapy (21).

The high percentage of patients with poor overall awareness (76.6%) is consistent with research from other developing countries, where health literacy regarding chronic diseases remains a challenge (22-24). However, the expressed interest in learning more about side effects, adherence, and medication mechanisms suggests that patients are willing to engage in education if provided. This finding is supported by studies showing that targeted patient counseling improves both knowledge and medication-taking behavior (25). The fact that only a minority received pharmacist-led lifestyle advice further highlights missed opportunities for multidisciplinary patient education, which is crucial in hypertension management (26).

Also, the current study showed significant limitations in how hypertensive patients in Saudi Arabia use and view pharmacy services. Many patients show limited interaction with pharmacists for managing their high blood pressure, with only a small fraction regularly seeking medication advice. This low engagement suggests that pharmacists aren't being used to their full potential in supporting the management of long-term conditions here, which aligns with observations from similar healthcare systems where pharmacists' clinical roles are often underutilized (27-29).

Patients had mixed feelings about how effective current pharmacy services are in helping them manage their blood pressure. This difference in opinion might originate from inconsistent service quality or varying levels of patient engagement. Patients clearly expressed a desire for more support, particularly concerning medication safety information, regular treatment reviews, and tools to help them stick to their medications. These preferences are in line with existing evidence indicating that comprehensive medication management can significantly improve blood pressure control (30, 31). The study also uncovered interesting trends in how patients prefer to receive support. While they weren't as keen on traditional one-on-one counseling, they showed greater interest in group education sessions and digital health solutions. This move towards more scalable and technology-driven approaches reflects global healthcare trends and points to opportunities for implementing innovative interventions that can reach more people (13, 17). The relatively low interest in printed materials might suggest a need for more interactive and personalized ways to educate patients.

These findings have important implications for healthcare delivery in Saudi Arabia. They highlight the need to broaden pharmacists' roles beyond simply dispensing medications to include structured patient education, regular follow-ups, and comprehensive medication management. The preference for digital solutions suggests potential benefits from incorporating mobile health technologies into hypertension care programs. Ultimately, these results indicate that reshaping pharmacy services to meet the needs identified by patients could significantly improve how high blood pressure is managed in primary care settings.

The improvements patients suggested for pharmacy services point to some really important ways we can enhance how hypertension is managed. A major theme was the need for more educational materials and making services easier to access, highlighting current gaps in patient support. Patients also reported the need for better training for pharmacists, particularly in managing hypertension. This suggests that current pharmacy education might need to better prepare pharmacists for their expanding roles in caring for people with chronic conditions. Furthermore, patients expressed a desire for more personalized follow-up, indicating they value having consistent care, which is known to improve outcomes for other long-term health issues.

Conclusions and Recommendations

In conclusion, this study revealed critical gaps in awareness, medication adherence, and the effective utilization of pharmacy services among hypertensive patients attending primary healthcare centers in Saudi Arabia. Despite being on long-term treatment, a significant portion of patients struggled with understanding their medications, faced adherence barriers, and reported limited engagement with pharmacists. These findings highlight an urgent need to strengthen the role of pharmacists in hypertension care, particularly in delivering education, monitoring adherence, and providing personalized follow-up. Pharmacists should be more actively integrated into patient care teams through routine counseling, structured medication reviews, and proactive follow-ups, especially for those on complex regimens. Also, targeted educational interventions, delivered via both group sessions and digital platforms, should be developed to improve patients' understanding of their medications, the importance of adherence, and when to seek help.

References

1. Al-Nozha MM, Abdullah M, Arafah MR, Khalil MZ, Khan NB, Al-Mazrou YY, Al-Maatouq MA, Al-Marzouki K, Al-Khadra A, Nouh MS, Al-Harthi SS. Hypertension in saudi arabia. Saudi medical journal. 2007 Jan 1;28(1):77.
2. Elbashir B, Al-dkheel M, Aldakheel H, Aruwished N, Alodayani N. Hypertension in Saudi Arabia: assessing life style and attitudes. International Journal of Translational Medical Research and Public Health. 2020 Feb 25;4(1):23-9.
3. Parati G, Lombardi C, Pengo M, Bilo G, Ochoa JE. Current challenges for hypertension management: From better hypertension diagnosis to improved patients' adherence and blood pressure control. International journal of cardiology. 2021 May 15; 331:262-9.
4. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. Nature Reviews Cardiology. 2021 Nov;18(11):785-802.
5. Burnier M, Damianaki A. Hypertension as cardiovascular risk factor in chronic kidney disease. Circulation research. 2023 Apr 14;132(8):1050-63.
6. Alqunaibet A, Herbst CH, El-Saharty S, Algwizani A, editors. Noncommunicable diseases in Saudi Arabia: toward effective interventions for prevention. World Bank Publications; 2021 Dec 6.
7. Al-Hanawi MK, Keetile M. Socio-economic and demographic correlates of non-communicable disease risk factors among adults in Saudi Arabia. Frontiers in Medicine. 2021 Apr 6; 8:605912.
8. Elendu C, Amaechi DC, Elendu TC, Amaechi EC, Elendu ID. Dependable approaches to hypertension management: A review. Medicine. 2024 Jun 14;103(24): e38560.
9. Burnier M, Egan BM. Adherence in hypertension: a review of prevalence, risk factors, impact, and management. Circulation research. 2019 Mar 29;124(7):1124-40.
10. Najimi A, Mostafavi F, Sharifirad G, Golshiri P. Barriers to medication adherence in patients with hypertension: A qualitative study. Journal of education and health promotion. 2018 Jan 1;7(1):24.
11. Celio J, Ninane F, Bugnon O, Schneider MP. Pharmacist-nurse collaborations in medication adherence-enhancing interventions: A review. Patient education and counseling. 2018 Jul 1;101(7):1175-92.
12. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nature Reviews Nephrology. 2020 Apr;16(4):223-37.
13. Al-Nozha MM, Abdullah M, Arafah MR, Khalil MZ, Khan NB, Al-Mazrou YY, Al-Maatouq MA, Al-Marzouki K, Al-Khadra A, Nouh MS, Al-Harthi SS. Hypertension in saudi arabia. Saudi medical journal. 2007 Jan 1;28(1):77.
14. AlHewiti A. Adherence to Long-term therapies and beliefs about medications. International journal of family medicine. 2014;2014(1):479596.
15. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, Jones DW, Materson BJ, Oparil S, Wright Jr JT, Roccella EJ. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. Jama. 2003 May 21;289(19):2560-71.
16. Maciel AP, Pimenta HB, Caldeira AP. Quality of life and medication adherence in hypertensive patients. ACTA Paulista De Enfermagem. 2016 Sep; 29:542-8.
17. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B. Interventions for enhancing medication adherence. Cochrane database of systematic reviews. 2014(11).
18. Aljumah K, Hassali MA. Impact of pharmacist intervention on adherence and measurable patient outcomes among depressed patients: a randomised controlled study. BMC psychiatry. 2015 Dec;15:1-9.
19. Alzahrani S, Alosaimi ME, Alamri AA, Alotaibi M, Almatar EA, Almanea BA, Aljabar SA, Alomar AS, Alzahrani AH, Al-Hindi ME, Al-Shams AA. Association between knowledge and drug adherence in patients with hypertension in Saudi Arabia. Archives of Pharmacy Practice. 2019;10(3-2019):71-6.
20. Bakhsh LA, Adas AA, Murad MA, Nourah RM, Hanbazazah SA, Aljahdali AA, Alshareef RJ. Awareness and knowledge on hypertension and its self-care practices among hypertensive patients in Saudi Arabia. Ann Int Med Dent Res. 2017;2(5):10-21276.
21. Kini V, Ho PM. Interventions to improve medication adherence: a review. Jama. 2018 Dec 18;320(23):2461-73.
22. Alsolami F, Correa-Velez I, Hou XY. Factors affecting antihypertensive medications adherence among hypertensive patients in Saudi Arabia. American Journal of Medicine and Medical Sciences. 2015 Jan 1;5(4):181-9.
23. Al-Hazmi AH, Alanazi AD, Thirunavukkarasu A, Alriwely NS, Alrais MM, Alruwaili AB, Alnosairi MS, Alsirhani AI. Evaluation of hypertension knowledge and its association with medication adherence among hypertensive patients attending primary health centers: a cross-sectional study from eastern Saudi Arabia. Frontiers in Public Health. 2025 Jan 13; 12:1378561.

24. Aldukhayel A, Saleh S, AlKhattaf AA, Aldawsari A. Impact of patients' knowledge of hypertension on adherence to antihypertensive drugs in Qassim region, Saudi Arabia. Medical Science. 2022;26.
25. Alaqeel S, Abanmy NO. Counselling practices in community pharmacies in Riyadh, Saudi Arabia: a cross-sectional study. BMC health services research. 2015 Jun; 15:1-9.
26. Carter BL, Rogers M, Daly J, Zheng S, James PA. The potency of team-based care interventions for hypertension: a meta-analysis. Archives of internal medicine. 2009 Oct 26;169(19):1748-55.
27. Cheema E, Sutcliffe P, Singer DRJ. The impact of pharmacist interventions in hypertension management. Br J Clin Pharmacol. 2014;78(6):1238-47.
28. Morgado M, Rolo S, Castelo-Branco M. Pharmacist intervention program to enhance hypertension control: a randomised controlled trial. International journal of clinical pharmacy. 2011 Feb; 33:132-40.
29. Chabot I, Moisan J, Grégoire JP, Milot A. Pharmacist intervention program for control of hypertension. Annals of Pharmacotherapy. 2003 Sep;37(9):1186-93.
30. Vawter L, Tong X, Gemilyan M, Yoon PW. Barriers to antihypertensive medication adherence among adults—United States, 2005. The Journal of Clinical Hypertension. 2008 Dec;10(12):922-9.
31. Kuo T, Chen S, Oh SM, Barragan NC, American Heart Association Western States Chronic Disease Prevention and Management Committee. Comprehensive medication management as a standard of practice for managing uncontrolled blood pressure. Frontiers in Medicine. 2021 Aug 3; 8:693171.

Red blood cell transfusions should be preserved just for emergencies in sickle cell diseases

Mehmet Rami Helvaci[1], Yusuf Aydin[1], Leyla Yilmaz Aydin[2], Alper Sevinc[1], Celaletdin Camci[1], Abdulrazak Abyad[3], Lesley Pocock[4]

(1) Specialist of Internal Medicine, MD, Turkey
(2) Specialist of Pulmonary Medicine, MD, Turkey
(3) Middle-East Academy for Medicine of Aging, MD, Lebanon
(4) Medi-WORLD International, Australia

Correspondence:
Prof Dr Mehmet Rami Helvaci
07400, ALANYA, Turkey
Phone: 00-90-506-4708759
Email: mramihelvaci@hotmail.com

Received: April 2025. Accepted: May 2025; Published:June 1, 2025.
Citation: Helvaci MR et al. Red blood cell transfusions should be preserved just for emergencies in sickle cell diseases. World Family Medicine. June 2025; 23(4): 40 - 53. DOI: 10.5742/MEWFM.2025.795257869

Abstract

Background: Atherosclerosis may be the main cause of aging and death.

Methods: All patients with sickle cell diseases (SCD) were included.

Results: We studied 222 males and 212 females with mean ages of 30.8 vs 30.3 years, p>0.05, respectively. Smoking (23.8% vs 6.1%, p<0.001), alcohol (4.9% vs 0.4%, p<0.001), transfused red blood cells (RBC) in their lifespans (48.1 vs 28.5 units, 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), chronic obstructive pulmonary disease (25.2% vs 7.0%, p<0.001), coronary heart disease (CHD) (18.0% vs 13.2%, p<0.05), leg ulcers (19.8% vs 7.0%, p<0.001), clubbing (14.8% vs 6.6%, p<0.001), chronic renal disease (9.9% vs 6.1%, p<0.05), and stroke (12.1% vs 7.5%, p<0.05) were all higher in males.

Conclusion: As an accelerated atherosclerotic process, hardened RBC-induced capillary endothelial damage initiating at birth terminates with multiorgan failures in early years of life in the SCD. Probably, stroke and CHD are the main causes of deaths even in the SCD. Probably, hydroxyurea is the most effective method of prevention of acute painful crises. On the other hand, RBC transfusions are the most effective treatments in acute painful crises both to decrease the severity of pain and to lower the risks of sudden deaths, probably due to the stroke or CHD, again. Because of the increased prevalences of allo-antibodies parallel to the increased number of transfusions, RBC transfusions should be preserved just for acute painful crises, surgical operations, births, and medical or surgical emergencies in the SCD.

Key words: Sickle cell diseases, capillary endothelial inflammation, acute painful crises, red blood cell transfusion, accelerated atherosclerosis, stroke, coronary heart disease

Introduction

Chronic endothelial damage may be the main cause of aging and death by means of atherosclerotic multiorgan insufficiencies in human being (1). Much higher blood pressures (BP) of the afferent vasculature may be the chief accelerating factor via recurrent injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are chiefly involved in the process. Therefore venosclerosis or phlebosclerosis is not as famous as atherosclerosis in medicine. Due to the chronic endothelial injury, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood supply to terminal organs, and increase systolic and decrease diastolic BP further. Some of the well-known accelerating factors of the inflammatory process are sedentary lifestyle, physical inactivity, animal-rich diet, emotional stresses, smoking, alcohol, excess fat tissue, chronic inflammations, prolonged infections, and cancers for the development of terminal consequences including obesity, hypertension (HT), diabetes mellitus (DM), coronary heart disease (CHD), cirrhosis, chronic obstructive pulmonary disease (COPD), 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 the above terminal consequences, after development of them, the endothelial changes can not be reversed, completely due to their fibrotic natures. The accelerating factors and terminal consequences of the vascular endothelial process are researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in medicine (4-6). Similarly, sickle cell diseases (SCD) are chronic inflammatory and destructive processes on vascular endothelium, initiating at birth and terminating with an accelerated atherosclerosis-induced multiorgan failures in much earlier ages (7, 8). Hemoglobin S causes loss of elastic and biconcave disc shaped structures of red blood cells (RBC). Probably loss of elasticity instead of shape is the main problem since sickling is rare in peripheric blood samples of cases with associated thalassemia minors (TM), and human survival is not affected in hereditary spherocytosis or elliptocytosis. Loss of elasticity is present during whole lifespan, but exaggerated with inflammations, infections, and additional stresses. The hardened RBC-induced chronic endothelial injury, inflammation, edema, and fibrosis terminate with tissue hypoxia in whole body (9). As a difference from other causes of chronic endothelial damage, SCD keep vascular endothelium particularly at the capillary level since the capillary system is the major distributor of the hardened RBC into the tissues (10, 11). The hardened RBC-induced chronic endothelial injury builds up an accelerated atherosclerosis in much earlier ages. Vascular narrowings and occlusions-induced tissue ischemia and multiorgan failures are the terminal consequences, so the mean life expectancy is decreased by 25 to 30 years for both genders in the SCD (8).

Material and Methods

The study was done in the Medical Faculty of the Mustafa Kemal University between March 2007 and June 2016. All cases with the SCD were studied. The SCD were diagnosed with the hemoglobin electrophoresis performed by means of high performance liquid chromatography (HPLC). Health histories including smoking, alcohol, acute painful crises per year, transfused units of RBC in their lifespans, leg ulcers, stroke, surgical procedures, 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 full physical examination was performed by the Same Internist, and cases with disseminated teeth losses (<20 teeth present) were noted. Patients with acute painful crises or other inflammatory events were treated at first, and the laboratory tests and clinical measurements were performed on the silent phase. Check up procedures including serum iron, iron binding capacity, ferritin, creatinine, liver function tests, markers of hepatitis viruses A, B, and C, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves, and to measure systolic BP 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 were performed. Other bones for avascular necrosis were scanned according to the patients' complaints. So avascular necrosis of bones was diagnosed via MRI (12). Associated TM were detected with serum iron, iron binding capacity, ferritin, and hemoglobin electrophoresis performed by means of HPLC because the SCD with associated TM come with milder clinics than the sickle cell anemia (SCA) (Hb SS) alone (13). Systolic BP of the pulmonary artery of 40 mmHg or greater are accepted as pulmonary hypertension (PHT) (14). Hepatic cirrhosis is diagnosed with full physical examination findings, laboratory parameters, and ultrasonographic evaluation. 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 detected clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum production, dyspnea, and hypoxia (16). An x-ray film of abdomen in upright position was taken just in patients with abdominal distention or discomfort, vomiting, obstipation, or lack of bowel movement, and ileus was diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity. CRD is diagnosed with a continuous serum creatinine level of 1.3 mg/dL or higher in males and 1.2 mg/dL or higher in females. Digital 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 taken in patients with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is performed for the exercise electrocardiogram positive patients. Eventually, CHD was

diagnosed either angiographically or with the Doppler echocardiographic findings as movement abnormalities in the walls of heart. Rheumatic heart disease is detected with the echocardiographic findings, too. Stroke is diagnosed by the CT and MRI of the brain. 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 used as 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), and there was no patient above the age of 59 years neither in males nor in females. Prevalences of associated TM were similar in males and females (72.5% vs 67.9%, p>0.05, respectively). Smoking (23.8% vs 6.1%) and alcohol (4.9% vs 0.4%) were both higher in males (p<0.001 for both) (Table 1). Transfused units of RBC in their lifespans (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), COPD (25.2% vs 7.0%, p<0.001), CHD (18.0% vs 13.2%, p<0.05), leg ulcers (19.8% vs 7.0%, p<0.001), digital clubbing (14.8% vs 6.6%, p<0.001), CRD (9.9% vs 6.1%, p<0.05), and stroke (12.1% vs 7.5%, p<0.05) were all higher in males, significantly. Although the mean age of mortality (30.2 vs 33.3 years) was lower in males, the difference was nonsignificant, probably due to the small sample size (Table 2). On the other hand, mean ages of the atherosclerotic consequences were shown in Table 3.

Table 1: Characteristic features of the study patients

Variables	Males with the SCD*	*p*-value	Females with the SCD
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 TM‡	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 minors

Table 2: Associated pathologies of the study patients

Variables	Males with the SCD*	*p*-value	Females with the SCD
Painful crises per year	5.0 ± 7.1 (0-36)	Ns†	4.9 ± 8.6 (0-52)
Transfused units of RBC‡	*48.1 ± 61.8 (0-434)*	*0.000*	*28.5 ± 35.8 (0-206)*
Disseminated teeth losses (<20 teeth present)	*5.4% (12)*	*<0.001*	*1.4% (3)*
CHD§	*18.0% (40)*	*<0.05*	*13.2% (28)*
Cirrhosis	*8.1% (18)*	*<0.001*	*1.8% (4)*
COPD¶	*25.2% (56)*	*<0.001*	*7.0% (15)*
Ileus	*7.2% (16)*	*<0.001*	*1.4% (3)*
Leg ulcers	*19.8% (44)*	*<0.001*	*7.0% (15)*
Digital clubbing	*14.8% (33)*	*<0.001*	*6.6% (14)*
*CRD***	*9.9% (22)*	*<0.05*	*6.1% (13)*
Stroke	*12.1% (27)*	*<0.05*	*7.5% (16)*
PHT***	12.6% (28)	Ns	11.7% (25)
Autosplenectomy	50.4% (112)	Ns	53.3% (113)
DVT**** and/or varices and/or telangiectasias	9.0% (20)	Ns	6.6% (14)
Rheumatic heart disease	6.7% (15)	Ns	5.6% (12)
Avascular necrosis of bones	24.3% (54)	Ns	25.4% (54)
Sickle cell retinopathy	0.9% (2)	Ns	0.9% (2)
Epilepsy	2.7% (6)	Ns	2.3% (5)
ACS*****	2.7% (6)	Ns	3.7% (8)
Mortality	7.6% (17)	Ns	6.6% (14)
Mean age of mortality (year)	30.2 ± 8.4 (19-50)	Ns	33.3 ± 9.2 (19-47)

*Sickle cell diseases †Nonsignificant (p>0.05) ‡Red blood cells §Coronary heart disease
¶Chronic obstructive pulmonary disease **Chronic renal disease ***Pulmonary hypertension
****Deep venous thrombosis *****Acute chest syndrome

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

Variables	Mean age (year)
Ileus	29.8 ± 9.8 (18-53)
Hepatomegaly	30.2 ± 9.5 (5-59)
ACS*	30.3 ± 10.0 (5-59)
Sickle cell retinopathy	31.5 ± 10.8 (21-46)
Rheumatic heart disease	31.9 ± 8.4 (20-49)
Autosplenectomy	32.5 ± 9.5 (15-59)
Disseminated teeth losses (<20 teeth present)	32.6 ± 12.7 (11-58)
Avascular necrosis of bones	32.8 ± 9.8 (13-58)
Epilepsy	33.2 ± 11.6 (18-54)
Priapism	33.4 ± 7.9 (18-51)
Left lobe hypertrophy of the liver	33.4 ± 10.7 (19-56)
Stroke	33.5 ± 11.9 (9-58)
COPD†	33.6 ± 9.2 (13-58)
PHT‡	34.0 ± 10.0 (18-56)
Leg ulcers	35.3 ± 8.8 (17-58)
Digital clubbing	35.4 ± 10.7 (18-56)
CHD§	35.7 ± 10.8 (17-59)
DVT¶ and/or varices and/or telangiectasias	37.0 ± 8.4 (17-50)
Cirrhosis	37.0 ± 11.5 (19-56)
CRD**	39.4 ± 9.7 (19-59)

Discussion

Excess weight may be the most common cause of vasculitis, and actually the term should be replaced with excess fat tissue in medicine. Probably, obesity is one of the endpoints of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide little benefit either to reverse obesity or to prevent its consequences. Excess fat leads to a chronic and low-grade inflammatory process on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess fat (19). The low-grade chronic inflammation may also cause genetic changes on the endothelial cells, and the systemic atherosclerosis may even decrease the clearance of malignant cells by natural killers (20). The chronic inflammatory process is characterized by lipid-induced injury, invasion of macrophages, proliferation of smooth muscle cells, endothelial dysfunction, and increased atherogenicity (21, 22). Excess fat is considered as a strong factor for controlling of C-reactive protein (CRP) concentration in serum, since excess fat tissue produces biologically active leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines (23, 24). On the other hand, individuals with excess fat will also have an increased cardiac output. The prolonged increase in blood volume may aggravate myocardial hypertrophy and decrease cardiac compliance further. Beside the systemic atherosclerosis and HT, fasting plasma glucose (FPG) and serum cholesterol increased and high density lipoproteins (HDL) decreased parallel to the increased body mass index (BMI) (25). Similarly, CHD and stroke increased parallel to the increased BMI (26). Eventually, the risk of death from all causes increased parallel to the severity of excess fat in all age groups, and the cases with underweight may even have lower biological ages and longer survival (27). Similarly, calorie restriction prolongs survival and retards age-related chronic diseases in human being (28).

Smoking may be the second most common cause of vasculitis. Probably, it causes a systemic inflammation on vascular endothelium terminating with an atherosclerosis-induced multiorgan failures in early years (29). Its atherosclerotic effect is obvious in Buerger's disease and COPD (30). Buerger's disease is an obliterative vasculitis in the small and medium-sized arteries and veins, and it has never been seen without smoking. Its characteristics are inflammation, fibrosis, and narrowing and occlusions of arteries and veins, predominantly in hands and feet. Claudication is the most common symptom with a severe pain caused by insufficient blood supply in feet and hands, particularly during exercise. It typically begins in extremities but it may also radiate to central areas in advanced cases. Numbness or tingling of the limbs is also common. Skin ulcerations and gangrene of fingers or toes are the final consequences. Similar to the venous ulcers, diabetic ulcers, leg ulcers of the SCD, clubbing, onychomycosis, and delayed wound and fracture healings of the lower extremities, pooling of blood due to the gravity may be important in the development of Buerger's disease, particularly in the lower extremities. Multiple narrowings and occlusions in the arms and legs are diagnostic in the angiogram. Skin biopsies are rarely needed because a

poorly perfused area will not heal, completely. Although most patients are heavy smokers, the limited smoking history of some patients may support the hypothesis that Buerger's disease may be an autoimmune reaction triggered by some constituent of tobacco. Although the only treatment way is complete cessation of smoking, the already developed narrowing and occlusions are irreversible. Due to the obvious role of inflammation, anti-inflammatory dose of aspirin in addition to the low-dose warfarin may be effective in prevention of microvascular infarctions of fingers and toes. On the other hand, FPG and HDL may be negative whereas triglycerides, low density lipoproteins (LDL), erythrocyte sedimentation rate, and CRP may be positive acute phase reactants in smokers (31). Similarly, smoking was associated with the lower BMI values due to the systemic inflammatory effects (32, 33). An increased heart rate was detected just after smoking even at rest (34). Nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (35). Nicotine may lengthen intermeal time, and decrease amount of meal eaten (36). 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 (37). Although the CHD was detected with similar prevalences in both genders, prevalences of smoking and COPD were higher in males against the higher prevalences of white coat hypertension, BMI, LDL, triglycerides, HT, and DM in females (38). The prevalence of myocardial infarction is increased three-fold in men and six-fold in women with smoking, so smoking may be more dangerous for women probably due to the higher BMI (39). Several toxic substances found in the cigarette smoke can affect various organ systems. For instance, smoking is usually associated with depression, irritable bowel syndrome (IBS), chronic gastritis, hemorrhoids, and urolithiasis with several mechanisms (40). First of all, smoking may have some antidepressive effects. Secondly, smoking-induced vascular inflammation may disturb epithelial functions for absorption and excretion in the gastrointestinal (GI) and genitourinary (GU) tracts (41). Thirdly, diarrheal losses-induced urinary changes may cause urolithiasis (42). Fourthly, smoking-induced sympathetic nervous system activation may cause motility problems in the GI and GU tracts terminating with IBS and urolithiasis. Eventually, immunosuppression secondary to smoking-induced vascular inflammation may terminate with the GI and GU tract infections causing urolithiasis since some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits. Actually, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced by the bacteria, producing urease. So, urolithiasis was seen in 17.9% of cases with IBS and 11.6% of cases without ($p<0.01$) (40).

Beside the stroke, CHD is the other terminal cause of death in human being. The most common triggering event is the disruption of an atherosclerotic plaque in an epicardial coronary artery, which leads to a clotting cascade. The plaque is a gradual and unstable collection of lipids, fibrous tissue, and white blood cells (WBC), particularly the macrophages in arterial walls in decades. Stretching and relaxation of arteries with each heart beat increases mechanical shear stress on atheromas to rupture. After the myocardial infarction, a collagen scar tissue takes its place which may also cause life threatening arrhythmias since the scar tissue conducts electrical impulses more slowly. The difference in conduction velocity between the injured and uninjured tissue can trigger re-entry or a feedback loop that is believed to be the cause of lethal arrhythmias. Ventricular fibrillation is the most serious arrhythmia that is the leading cause of sudden cardiac death. It is an extremely fast and chaotic heart rhythm. Ventricular tachycardia may also cause sudden cardiac death that usually results in rapid heart rates preventing effective cardiac pumping. Cardiac output and BP may fall to dangerous levels which can lead to further coronary ischemia and extension of the infarct. This scar tissue may even cause ventricular aneurysm, rupture, and sudden cardiac death. Aging, physical inactivity, sedentary lifestyle, animal-rich diet, excess fat tissue, emotional stresses, smoking, alcohol, prolonged infections, chronic inflammations, and cancers are important in atherosclerotic plaque formation. Moderate physical exercise is associated with a 50% reduced incidence of CHD (43). Probably, excess fat tissue may be the most important cause of CHD since there are nearly 20 kg of excess fat tissue between the lower and upper borders of normal weight, 33 kg between the obesity, 66 kg between the morbid obesity (BMI ≥ 40 kg/m2), and 81 kg between the super obesity (BMI ≥ 45 kg/m2) in adults. In fact, there is a huge percentage of adults with a heavier fat mass than their organ plus muscle masses that brings a heavy stress both on the heart and brain.

Cirrhosis is 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, globally. 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 at the moment (44). NAFLD is a marker of pathological fat deposition combined with a low-grade inflammation that results with hypercoagulability, endothelial dysfunction, and an accelerated atherosclerosis (44). Beside terminating with cirrhosis, NAFLD is associated with higher overall mortality rates as well as increased prevalences of CHD and stroke (45). Authors reported independent associations between NAFLD and impaired flow-mediated vasodilation and increased mean carotid artery intima-media thickness (CIMT) (46). NAFLD may be considered as one of the hepatic consequences of the metabolic syndrome and SCD (47). Probably smoking also takes role in the inflammatory process of the capillary endothelium in the liver because the systemic inflammatory effects of smoking on the endothelial cells is obvious in Buerger's disease and COPD (36). Increased oxidative stress, inactivation of antiproteases, and release of proinflammatory mediators may terminate with the systemic atherosclerosis in smokers. The atherosclerotic

effects of alcohol is more prominent in hepatic endothelium probably due to the highest concentrations of its metabolites in the liver. Chronic infectious and inflammatory processes and cancers may also terminate with an accelerated atherosclerotic process (48). 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 (49). As a result, cirrhosis may also be another atherosclerotic consequence of the metabolic syndrome and SCD, again.

Acute painful crises are the severest symptoms of the SCD. 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 (50). The increased basal metabolic rate during such stresses aggravates the sickling, capillary endothelial damage, inflammation, edema, tissue hypoxia, and multiorgan insufficiencies. So the risk of mortality is much higher during such crises. Actually, each crisis may complicate with the following crises by leaving sequelaes on the capillary endothelial system in whole body. After a period of time, the sequelaes may terminate with sudden multiorgan failures and death with a final crisis that may even not be severe, clinically. Similarly, after a 20-year experience on such patients, the deaths seem sudden and unexpected events in the SCD. Unfortunately, most of the deaths develop just after the hospital admission, and majority of them are patients without hydroxyurea therapy (51, 52). Rapid RBC supports are usually life-saving for such patients, although preparation of RBC units for transfusion usually takes time. Beside that RBC supports in emergencies become much more difficult in terminal cases due to the repeated transfusions-induced blood group mismatch. Actually, transfusion of each unit of RBC complicates the following transfusions by means of the blood subgroup mismacth. Due to the significant efficacy of hydroxyurea therapy, RBC transfusions should be preserved just for for acute painful crises, surgical operations, births, and medical or surgical emergencies in the SCD (51, 52). According to our experiences, simple and repeated transfusions are superior to RBC exchange in the SCD (53, 54). First of all, preparation of one or two units of RBC 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 patients. Secondly, transfusions of one or two units of RBC suspensions in each time decrease the severity of pain, and relax anxiety of the patients and their relatives since RBC transfusions probably have the strongest analgesic effects during the crises (55). Actually, the decreased severity of pain by transfusions also indicates the decreased severity of inflammation all over the body. Thirdly, transfusions of lesser units of RBC suspensions in each time by means of the simple transfusions will decrease transfusion-related complications including infections, iron overload, and blood group mismatch in the future. Fourthly, transfusion of RBC suspensions in the secondary health centers may prevent some deaths developed during the transport to the tertiary centers for the exchange. Finally, cost of the simple 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 RBC, WBC, platelets (PLT), and endothelial cells, yet. Whether leukocytosis contributes to the pathogenesis by releasing cytotoxic enzymes is unknown. The adverse effects of WBC on vascular endothelium are of particular interest for atherosclerotic consequences in the SCD. For example, leukocytosis even in the absence of any infection was an independent predictor of the severity of the SCD (56), and it was associated with the risk of stroke (57). Disseminated tissue hypoxia, releasing of inflammatory mediators, bone infarctions, and activation of afferent nerves may take role in the pathophysiology of the intolerable pain. Due to the severity of pain, narcotic analgesics are usually needed (58), but according to our practice, simple and repeated RBC transfusions may be highly effective both to relieve pain and to prevent sudden deaths that may develop secondary to the stroke or CHD on the chronic atherosclerotic background of the SCD, again.

Hydroxyurea may be the only life-saving drug for the treatment of the SCD. 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 suppression of leukocytosis and thrombocytosis by blocking the DNA synthesis in the SCD (59, 60). By this way, the chronic inflammatory and destructive process of the SCD 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 in the viral hepatitis cases, although presence of a continuous damage of sickle cells on the capillary endothelium, the severity of destructive process is probably exaggerated by the patients' own WBC and PLT. So suppression of proliferation of them may limit the endothelial damage-induced edema, ischemia, and infarctions in whole body (61). Similarly, final Hb F levels in hydroxyurea users did not differ from their pretreatment levels (62). 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 (63). The study particularly researched effects of hydroxyurea on painful crises, ACS, and requirement of blood transfusion. The outcomes were so overwhelming in the favour of hydroxyurea that the study was terminated after 22 months, and hydroxyurea was initiated for all patients. The MSH also demonstrated that patients treated with hydroxyurea had a 44% decrease in hospitalizations (63). In multivariable analyses, there was a strong and independent association of lower neutrophil counts with the lower crisis rates (63). 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 (63). Whereas we used all subtypes of the SCD 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) (51). Parallel to us, adult patients using hydroxyurea for frequent painful crises appear to have reduced mortality rate after a 9-year follow-up period (64). Although the underlying disease severity remains critical to determine prognosis, hydroxyurea may also decrease severity of disease and prolong survival (64). The complications start to be seen even in infancy in the SCD. For example, infants with lower hemoglobin values were more likely to have higher incidences of ACS, painful crises, and lower neuropsychological scores, and hydroxyurea reduced the incidences of them (65). If started in early years of life, hydroxyurea may protect splenic function, improve growth, and prevent multiorgan insufficiencies. Although RBC transfusions can also reduce the complications, there are the risks of infections, iron overload, and development of allo-antibodies causing subsequent transfusions much more difficult. Therefore RBC transfusions should be kept in hands just for emergencies as the most effective weapon at the moment.

Aspirin is a member of nonsteroidal anti-inflammatory drugs (NSAID). Although aspirin has similar anti-inflammatory effects with the other NSAID, it also suppresses the normal functions of PLT, irreversibly. This property causes aspirin being different from other NSAID, 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 inactivates the COX enzyme, irreversibly, which is required for the synthesis of prostaglandins (PG) and thromboxanes (TX). PG 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. TX are responsible for the aggregation of PLT to form blood clots. In another definition, low-dose aspirin irreversibly blocks the formation of TXA2 in the PLT, producing an inhibitory effect on the PLT aggregation during whole lifespan of the affected PLT (8-9 days). Since PLT do not have nucleus and DNA, they are unable to synthesize new COX enzyme once aspirin has inhibited the enzyme. But aspirin does not decrease the blood viscosity. The antithrombotic property of aspirin is useful to reduce the risks of myocardial infarction, transient ischemic attack, and stroke (66). 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 (67). According to the literature, aspirin may also be effective in prevention of colorectal cancers (68). On the other hand, aspirin has some side effects including gastric ulcers, gastric bleeding, worsening of asthma, and Reye syndrome in childhood and adolescence. Due to the risk of Reye syndrome, the US Food and Drug Administration recommends that aspirin should not be prescribed for febrile patients under the age of 12 years (69). Eventually, the general recommendation to use aspirin in children has been withdrawn, and it was only recommended for Kawasaki disease (70). Reye syndrome is a rapidly worsening brain disease (70). The first detailed description of Reye syndrome was in 1963 by an Australian pathologist, Douglas Reye (71). The syndrome mostly affects children, but it can only affect fewer than one in a million children a year (71). Symptoms of Reye syndrome may include personality changes, confusion, seizures, and loss of consciousness (70). Although the liver toxicity typically occurs in the syndrome, jaundice is usually not seen with it, but the liver is enlarged in most cases (70). Although the death occurs in 20-40% of affected cases, about one third of survivors get a significant degree of brain damage (70). It usually starts just after recovery from a viral infection, such as influenza or chicken pox. About 90% of cases in children are associated with an aspirin use (71, 72). Inborn errors of metabolism are also the other risk factors, and the genetic testing for inborn errors of metabolism became available in developed countries in the 1980s (70). When aspirin use was withdrawn for children in the US and UK in the 1980s, a decrease of more than 90% in rates of Reye syndrome was seen (71). The treatment is supportive. Mannitol can be used for the brain swelling (71). Due to the very low risk of Reye syndrome but much higher risk of death due to the SCD in children, aspirin should be added both into the acute and chronic phase treatments with an anti-inflammatory dose even in childhood in the SCD (73).

Warfarin is an anticoagulant, and it is found in the List of Essential Medicines of WHO. In 2020, it was the 58th most commonly prescribed medication in the United States. It does not reduce blood viscosity. Warfarin is used to decrease the tendency for thrombosis, and it can prevent formation of blood clots and reduce the risk of embolism. Warfarin is the best suited for anticoagulation in areas of slowly flowing blood such as in veins and the pooled blood behind artificial and natural valves, and in blood pooled in dysfunctional cardiac atria. It is commonly used to prevent blood clots in the circulatory system such as DVT and pulmonary embolism, and to protect against stroke in atrial fibrillation (AF), valvular heart disease, or artificial heart valves. Less commonly, it is used following ST-segment elevation myocardial infarction and orthopedic surgery. The warfarin initiation regimens are simple, safe, and suitable to be used in ambulatory and in patient settings (74). Warfarin should be initiated with a 5 mg dose, or 2 to 4 mg in the elderlies. In the protocol of low-dose warfarin, the target international normalised ratio (INR) value is between 2.0 and 2.5, whereas in the protocol of standard-dose warfarin, the target INR value is between 2.5 and 3.5 (75). When warfarin is used and INR is in therapeutic range, simple discontinuation of the drug for five days is enough to reverse the effect, and causes INR to drop below 1.5 (76). Its effects can be reversed with phytomenadione (vitamin K1), fresh frozen plasma, or prothrombin complex concentrate, rapidly. Blood products should not be routinely used to reverse warfarin overdose, when vitamin K1 could work alone. Warfarin decreases blood clotting by blocking vitamin K epoxide reductase, an ezyme that reactivates vitamin K1. Without sufficient active vitamin K1, clotting factors II, VII, IX, and X have decreased clotting ability. The

anticlotting protein C and protein S are also inhibited, but to a lesser degree. A few days are required for full effect to occur, and these effects can last for up to five days. The consensus agrees that current self-testing and management devices are effective methods of monitoring oral anticoagulation therapy, providing outcomes possibly better than achieved, clinically. The only common side effect of warfarin is hemorrhage. The risk of severe bleeding is low with a yearly rate of 1-3% (77). All types of bleeding may occur, but the severest ones are those involving the central nervous system (76). The risk is particularly increased once the INR exceeds 4.5 (77). The risk of bleeding is increased further when warfarin is combined with antiplatelet drugs such as clopidogrel or aspirin (78). But thirteen publications from 11 cohorts including more than 48.500 patients with more than 11.600 warfarin users were included in the meta-analysis (79). In patients with AF and non-end-stage CRD, warfarin resulted in a lower risk of ischemic stroke ($p= 0.004$) and mortality ($p<0.00001$), but had no effect on major bleeding ($p>0.05$) (79). Similarly, warfarin is associated with significant reductions in ischemic stroke even in patients with warfarin-associated intracranial hemorrhage (ICH) (80). Whereas recurrent ICH occured in 6.7% of patients who used warfarin and 7.7% of patients who did not use warfarin without any significant difference in between ($p>0.05$) (80). On the other hand, patients with cerebral venous thrombosis (CVT) those were anticoagulated either with warfarin or dabigatran had low risk of recurrent venous thrombotic events (VTE), and the risk of bleeding was similar in both regimens, suggesting that both warfarin and dabigatran are safe and effective for preventing recurrent VTE in cases with CVT (81). Additionally, an INR value of 1.5 achieved with an average daily dose of 4.6 mg warfarin, has resulted in no increase in the number of men ever reporting minor bleeding episodes (82). Non-rheumatic AF increases the risk of stroke, presumably from atrial thromboemboli, and long-term low-dose warfarin therapy is highly effective and safe in preventing stroke in them (83). There were just two strokes in the warfarin group (0.41% per year) as compared with 13 strokes in the control group (2.98% per year) with a reduction of 86% in the risk of stroke ($p= 0.0022$) (83). The mortality was markedly lower in the warfarin group, too ($p= 0.005$) (83). The frequencies of bleedings that required hospitalization or transfusion were the same in both groups ($p>0.05$) (83). Additionally, very-low-dose warfarin was safe and effective for prevention of thromboembolism in metastatic breast cancer (84). The average daily dose was 2.6 mg, and the mean INR was 1.5 (84). On the other hand, new oral anticoagulants had a favourable risk-benefit profile with significant reductions in stroke, ICH, and mortality, and with similar major bleedings as for warfarin, but increased GI bleeding (85). Interestingly, rivaroxaban and low-dose apixaban were associated with increased risks of all cause mortality compared with warfarin (86). The mortality rates were 4.1%, 3.7%, and 3.6% per year in the warfarin, 110 mg of dabigatran, and 150 mg of dabigatran groups ($p>0.05$ for both) in AF in another study, respectively (87). On the other hand, infections, medical or surgical emergencies, and emotional stresses-induced increased basal metabolic rate accelerates sickling, and an exaggerated capillary endothelial edema-induced myocardial infarction and stroke may cause sudden deaths (88). So lifelong aspirin with an anti-inflammatory dose plus low-dose warfarin may be a life-saving regimen even at childhood to decrease severity of capillary inflammation and to prevent thromboembolic events in the SCD (89).

COPD is the third leading cause of death in the world (90, 91). Aging, smoking, alcohol, male gender, excess fat tissue, chronic inflammations, prolonged infections, and cancers may be the major causes. Atherosclerotic effects of smoking may be the most obvious in the COPD and Buerger's disease, probably due to the higher concentrations of toxic substances in the lungs and pooling of blood in the extremities. After smoking, excess fat tissue may be the second common cause of COPD due to the excess fat tissue-induced atherosclerotic process in whole body. Regular alcohol consumption may be the third leading cause of the systemic accelerated atherosclerotic process and COPD, since COPD was one of the most common diagnoses in alcohol dependence (92). Furthermore, 30-day readmission rates were higher in the COPD patients with alcoholism (93). Probably an accelerated atherosclerotic process is the main structural background of functional changes that are characteristics of 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 actually 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 (94). For example, there may be close relationships between COPD, CHD, PAD, and stroke (95). Furthermore, two-third of mortality cases were caused by cardiovascular diseases and lung cancers in the COPD, and the CHD was the most common cause in a multi-center study of 5.887 smokers (96). When the hospitalizations were researched, the most common causes were the cardiovascular diseases, again (96). In another study, 27% of mortality cases were due to the cardiovascular diseases in the moderate and severe COPD (97). On the other hand, COPD may be the pulmonary consequence of the systemic atherosclerotic process caused by the hardened RBC in the SCD (90).

Leg ulcers are seen in 10% to 20% of the SCD (98). Its prevalence increases with aging, male gender, and SCA (99). The leg ulcers have an intractable nature, and around 97% of them relapse in a period of one year (98). Similar to Buerger's disease, the leg ulcers occur in the distal segments of the body with a lesser collateral blood flow (98). The hardened RBC-induced chronic endothelial damage, inflammation, edema, and fibrosis at the capillaries may be the major causes (99). Prolonged exposure to the hardened bodies due to the pooling of blood in the lower extremities may also explain the leg but not arm ulcers in the SCD. The hardened RBC-induced venous insufficiencies may also accelerate the process by pooling of causative bodies in the legs, and vice versa. Pooling of blood may also be

important for the development of venous ulcers, diabetic ulcers, Buerger's disease, clubbing, and onychomycosis in the lower extremities. Furthermore, pooling of blood may be the 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. Hydroxyurea is the first drug that was approved by Food and Drug Administration in the SCD (100). It is an oral, cheap, safe, and effective drug that blocks cell division by suppressing formation of deoxyribonucleotides which are the building blocks of DNA (11). Its main action may be the suppression of hyperproliferative WBC and PLT in the SCD (101). Although presence of a continuous damage of hardened RBC on vascular endothelium, severity of the destructive process is probably exaggerated by immune systems. Similarly, lower WBC counts were associated with lower crises rates, and if a tissue infarct occurs, lower WBC counts may decrease severity of tissue damage and pain (62). Prolonged resolution of leg ulcers with hydroxyurea may also suggest that the ulcers may be secondary to increased WBC and PLT counts-induced exaggerated capillary endothelial inflammation and edema.

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 (102). Although the exact cause and significance is unknown, the chronic tissue hypoxia is highly suspected (103). 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, and hepatic diseases and smoking which are characterized with chronic tissue hypoxia (5). As an explanation for that hypothesis, lungs, heart, kidneys, and liver are closely related organs which affect their functions in a short period of time. On the other hand, digital clubbing is also common in the SCD, 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 capillary level in the SCD. Beside the effects of SCD, 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 role of male gender in the systemic atherosclerotic process.

CRD is also increasing all over the world that can also be explained by aging of the human being and increased prevalence of excess weight (104). Aging, animal-rich diet, excess fat tissue, smoking, alcohol, inflammatory and infectious processes, and cancers may be the major 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 (105). Excess fat tissue-induced hyperglycemia, dyslipidemia, elevated BP, and insulin resistance can cause tissue inflammation and immune cell activation (106). For example, age ($p= 0.04$), high-sensitivity CRP ($p= 0.01$), mean arterial BP ($p= 0.003$), and DM ($p= 0.02$) had significant correlations with the CIMT (104). 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 BP with excess weight (107). Excess fat tissue also causes renal vasodilation and glomerular hyperfiltration which initially serve as compensatory mechanisms to maintain sodium balance due to the increased tubular reabsorption (107). However, along with the increased BP, these changes cause a hemodynamic burden on the kidneys in long term that causes chronic endothelial damage (108). With prolonged excess fat tissue, there are increased urinary protein excretion, loss of nephron function, and exacerbated HT. With the development of dyslipidemia and DM, CRD progresses much more easily (107). On the other hand, the systemic inflammatory effects of smoking on endothelial cells may also be important in the CRD (109). Although some authors reported that alcohol was not related with the CRD (109), various metabolites of alcohol circulate in blood vessels of kidneys and give harm to the endothelium. Chronic inflammatory and infectious processes may also terminate with the accelerated atherosclerosis in the renal vasculature (108). Due to the systemic nature of atherosclerosis, there are close relationships between CRD and other atherosclerotic consequences of the metabolic syndrome including CHD, COPD, PAD, cirrhosis, and stroke (110, 111). For example, the most common causes of death were the CHD and stroke in the CRD again (112). The hardened RBC-induced capillary endothelial damage may be the main cause of CRD in the SCD, again (113).

Beside the CHD, stroke is the other terminal cause of death, and it develops as an acute thromboembolic event on the chronic atherosclerotic background. Aging, male gender, smoking, alcohol, and excess fat tissue may be the major underlying causes. Stroke is also a common complication of the SCD (114). Similar to the leg ulcers, stroke is particularly higher in the SCA and cases with higher WBC counts (115). Sickling-induced capillary endothelial damage, activations of WBC, PLT, and coagulation system, and hemolysis may terminate with chronic capillary endothelial inflammation, edema, and fibrosis (116). Probably, stroke may not have a macrovascular origin in the SCD, and diffuse capillary endothelial inflammation, edema, and fibrosis may be much more important. Infections, inflammations, medical or surgical emergencies, and emotional stress 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 due to the increased WBC and PLT counts-induced capillary endothelial inflammation and edema (117).

As a conclusion, hardened RBC-induced capillary endothelial damage initiating at birth terminates with multiorgan failures in early years of life in the SCD. Probably, stroke and CHD are the main causes of deaths even in the SCD. Probably, hydroxyurea is the most

effective method of prevention of acute painful crises. On the other hand, RBC transfusions are the most effective treatments in acute painful crises both to decrease the severity of pain and to lower the risks of sudden deaths, probably due to the stroke or CHD, again. Due to the increased prevalences of allo-antibodies parallel to the increased number of transfusions, RBC transfusions should be preserved just for acute painful crises, surgical operations, births, and medical or surgical emergencies in the SCD.

References

1. Widlansky ME, Gokce N, Keaney JF Jr, Vita JA. The clinical implications of endothelial dysfunction. J Am Coll Cardiol 2003; 42(7): 1149-60.
2. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365(9468): 1415-28.
3. Franklin SS, Barboza MG, Pio JR, Wong ND. Blood pressure categories, hypertensive subtypes, and the metabolic syndrome. J Hypertens 2006; 24(10): 2009-16.
4. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106(25): 3143-421.
5. Helvaci MR, Aydin LY, Aydin Y. Digital clubbing may be an indicator of systemic atherosclerosis even at microvascular level. HealthMED 2012; 6(12): 3977-81.
6. Anderson RN, Smith BL. Deaths: leading causes for 2001. Natl Vital Stat Rep 2003; 52(9): 1-85.
7. Helvaci MR, Gokce C, Davran R, Akkucuk S, Ugur M, Oruc C. Mortal quintet of sickle cell diseases. Int J Clin Exp Med 2015; 8(7): 11442-8.
8. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. N Engl J Med 1994; 330(23): 1639-44.
9. Helvaci MR, Yaprak M, Abyad A, Pocock L. Atherosclerotic background of hepatosteatosis in sickle cell diseases. World Family Med 2018; 16(3): 12-8.
10. Helvaci MR, Kaya H. Effect of sickle cell diseases on height and weight. Pak J Med Sci 2011; 27(2): 361-4.
11. Helvaci MR, Aydin Y, Ayyildiz O. Hydroxyurea may prolong survival of sickle cell patients by decreasing frequency of painful crises. HealthMED 2013; 7(8): 2327-32.
12. Mankad VN, Williams JP, Harpen MD, Manci E, Longenecker G, Moore RB, et al. Magnetic resonance imaging of bone marrow in sickle cell disease: clinical, hematologic, and pathologic correlations. Blood 1990; 75(1): 274-83.
13. Helvaci MR, Aydin Y, Ayyildiz O. Clinical severity of sickle cell anemia alone and sickle cell diseases with thalassemias. HealthMED 2013; 7(7): 2028-33.
14. Fisher MR, Forfia PR, Chamera E, Housten-Harris T, Champion HC, Girgis RE, et al. Accuracy of Doppler echocardiography in the hemodynamic assessment of pulmonary hypertension. Am J Respir Crit Care Med 2009; 179(7): 615-21.
15. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013; 187(4): 347-65.
16. Davies SC, Luce PJ, Win AA, Riordan JF, Brozovic M. Acute chest syndrome in sickle-cell disease. Lancet 1984; 1(8367): 36-8.
17. Vandemergel X, Renneboog B. Prevalence, aetiologies and significance of clubbing in a department of general internal medicine. Eur J Intern Med 2008; 19(5): 325-9.
18. Schamroth L. Personal experience. S Afr Med J 1976; 50(9): 297-300.
19. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999; 341(15): 1097-105.
20. Helvaci MR, Aydin Y, Gundogdu M. Smoking induced atherosclerosis in cancers. HealthMED 2012; 6(11): 3744-9.
21. Ross R. Atherosclerosis--an inflammatory disease. N Engl J Med 1999; 340(2): 115-26.
22. Ridker PM. High-sensitivity C-reactive protein: Potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001; 103(13): 1813-8.
23. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA 1998; 279(18): 1477-82.
24. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. JAMA 1999; 282(22): 2131-5.
25. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. Obes Rev 2002; 3(3): 147-56.
26. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. Biomed Environ Sci 2002; 15(3): 245-52.
27. Helvaci MR, Kaya H, Yalcin A, Kuvandik G. Prevalence of white coat hypertension in underweight and overweight subjects. Int Heart J 2007; 48(5): 605-13.
28. Heilbronn LK, Ravussin E. Calorie restriction and aging: review of the literature and implications for studies in humans. Am J Clin Nutr 2003; 78(3): 361-9.
29. Fodor JG, Tzerovska R, Dorner T, Rieder A. Do we diagnose and treat coronary heart disease differently in men and women? Wien Med Wochenschr 2004; 154(17-18): 423-5.
30. Helvaci MR, Aydin LY, Aydin Y. Chronic obstructive pulmonary disease may be one of the terminal end points of metabolic syndrome. Pak J Med Sci 2012; 28(3): 376-9.
31. Helvaci MR, Kayabasi Y, Celik O, Sencan H, Abyad A, Pocock L. Smoking causes a moderate or severe inflammatory process in human body. Am J Biomed Sci & Res 2023; 7(6): 694-702.

32. Grunberg NE, Greenwood MR, Collins F, Epstein LH, Hatsukami D, Niaura R, et al. National working conference on smoking and body weight. Task Force 1: Mechanisms relevant to the relations between cigarette smoking and body weight. Health Psychol 1992; 11: 4-9.
33. Helvaci MR, Camci C, Nisa EK, Ersahin T, Atabay A, Alrawii I, Ture Y, Abyad A, Pocock L. Severity of sickle cell diseases restricts smoking. Ann Med Medical Res 2024; 7: 1074.
34. Walker JF, Collins LC, Rowell PP, Goldsmith LJ, Moffatt RJ, Stamford BA. The effect of smoking on energy expenditure and plasma catecholamine and nicotine levels during light physical activity. Nicotine Tob Res 1999; 1(4): 365-70.
35. Hughes JR, Hatsukami DK. Effects of three doses of transdermal nicotine on post-cessation eating, hunger and weight. J Subst Abuse 1997; 9: 151-9.
36. Miyata G, Meguid MM, Varma M, Fetissov SO, Kim HJ. Nicotine alters the usual reciprocity between meal size and meal number in female rat. Physiol Behav 2001; 74(1-2): 169-76.
37. Froom P, Melamed S, Benbassat J. Smoking cessation and weight gain. J Fam Pract 1998; 46(6): 460-4.
38. Helvaci MR, Kaya H, Gundogdu M. Gender differences in coronary heart disease in Turkey. Pak J Med Sci 2012; 28(1): 40-4.
39. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J. Smoking and risk of myocardial infarction in women and men: longitudinal population study. BMJ 1998; 316(7137): 1043-7.
40. Helvaci MR, Kabay S, Gulcan E. A physiologic events' cascade, irritable bowel syndrome, may even terminate with urolithiasis. J Health Sci 2006; 52(4): 478-81.
41. Helvaci MR, Dede G, Yildirim Y, Salaz S, Abyad A, Pocock L. Smoking may even cause irritable bowel syndrome. World Family Med 2019; 17(3): 28-33.
42. Helvaci MR, Algin MC, Kaya H. Irritable bowel syndrome and chronic gastritis, hemorrhoid, urolithiasis. Eurasian J Med 2009; 41(3): 158-61.
43. Kamimura D, Loprinzi PD, Wang W, Suzuki T, Butler KR, Mosley TH, et al. Physical activity is associated with reduced left ventricular mass in obese and hypertensive African Americans. Am J Hypertens 2017; 30(6): 617-23.
44. Bhatia LS, Curzen NP, Calder PC, Byrne CD. Non-alcoholic fatty liver disease: a new and important cardiovascular risk factor? Eur Heart J 2012; 33(10): 1190-1200.
45. Pacifico L, Nobili V, Anania C, Verdecchia P, Chiesa C. Pediatric nonalcoholic fatty liver disease, metabolic syndrome and cardiovascular risk. World J Gastroenterol 2011; 17(26): 3082-91.
46. Mawatari S, Uto H, Tsubouchi H. Chronic liver disease and arteriosclerosis. Nihon Rinsho 2011; 69(1): 153-7.
47. Bugianesi E, Moscatiello S, Ciaravella MF, Marchesini G. Insulin resistance in nonalcoholic fatty liver disease. Curr Pharm Des 2010; 16(17): 1941-51.
48. Mostafa A, Mohamed MK, Saeed M, Hasan A, Fontanet A, Godsland I, et al. Hepatitis C infection and clearance: impact on atherosclerosis and cardiometabolic risk factors. Gut 2010; 59(8): 1135-40.
49. Helvaci MR, Ayyildiz O, Gundogdu M, Aydin Y, Abyad A, Pocock L. Hyperlipoproteinemias may actually be acute phase reactants in the plasma. World Family Med 2018; 16(1): 7-10.
50. Parfrey NA, Moore W, Hutchins GM. Is pain crisis a cause of death in sickle cell disease? Am J Clin Pathol 1985; 84: 209-12.
51. Helvaci MR, Ayyildiz O, Gundogdu M. Hydroxyurea therapy and parameters of health in sickle cell patients. HealthMED 2014; 8(4): 451-6.
52. Helvaci MR, Tonyali O, Yaprak M, Abyad A, Pocock L. Increased sexual performance of sickle cell patients with hydroxyurea. World Family Med 2019; 17(4): 28-33.
53. Helvaci MR, Atci N, Ayyildiz O, Muftuoglu OE, Pocock L. Red blood cell supports in severe clinical conditions in sickle cell diseases. World Family Med 2016; 14(5): 11-8.
54. Helvaci MR, Ayyildiz O, Gundogdu M. Red blood cell transfusions and survival of sickle cell patients. HealthMED 2013; 7(11): 2907-12.
55. Helvaci MR, Cayir S, Halici H, Sevinc A, Camci C, Abyad A, Pocock L. Red blood cell transfusions may have the strongest analgesic effect during acute painful crises in sickle cell diseases. Ann Clin Med Case Rep 2024; V13(12): 1-12.
56. Miller ST, Sleeper LA, Pegelow CH, Enos LE, Wang WC, Weiner SJ, et al. Prediction of adverse outcomes in children with sickle cell disease. N Engl J Med 2000; 342: 83-9.
57. Balkaran B, Char G, Morris JS, Thomas PW, Serjeant BE, Serjeant GR. Stroke in a cohort of patients with homozygous sickle cell disease. J Pediatr 1992; 120: 360-6.
58. Cole TB, Sprinkle RH, Smith SJ, Buchanan GR. Intravenous narcotic therapy for children with severe sickle cell pain crisis. Am J Dis Child 1986; 140: 1255-9.
59. Miller BA, Platt O, Hope S, Dover G, Nathan DG. Influence of hydroxyurea on fetal hemoglobin production in vitro. Blood 1987; 70(6): 1824-9.
60. Platt OS. Is there treatment for sickle cell anemia? N Engl J Med 1988; 319(22): 1479-80.
61. Helvaci MR, Aydogan F, Sevinc A, Camci C, Dilek I. Platelet and white blood cell counts in severity of sickle cell diseases. Pren Med Argent 2014; 100(1): 49-56.
62. Charache S. Mechanism of action of hydroxyurea in the management of sickle cell anemia in adults. Semin Hematol 1997; 34(3): 15-21.
63. Charache S, Barton FB, Moore RD, Terrin ML, Steinberg MH, Dover GJ, et al. Hydroxyurea and sickle cell anemia. Clinical utility of a myelosuppressive "switching" agent. The Multicenter Study of Hydroxyurea in Sickle Cell Anemia. Medicine (Baltimore) 1996; 75(6): 300-26.
64. Steinberg MH, Barton F, Castro O, Pegelow CH, Ballas SK, Kutlar A, et al. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. JAMA 2003; 289(13): 1645-51.

65. Lebensburger JD, Miller ST, Howard TH, Casella JF, Brown RC, Lu M, et al; BABY HUG Investigators. Influence of severity of anemia on clinical findings in infants with sickle cell anemia: analyses from the BABY HUG study. Pediatr Blood Cancer 2012; 59(4): 675-8.
66. Toghi H, Konno S, Tamura K, Kimura B, Kawano K. Effects of low-to-high doses of aspirin on platelet aggregability and metabolites of thromboxane A2 and prostacyclin. Stroke 1992; 23(10): 1400-3.
67. Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009; 373(9678): 1849-60.
68. Algra AM, Rothwell PM. Effects of regular aspirin on long-term cancer incidence and metastasis: a systematic comparison of evidence from observational studies versus randomised trials. Lancet Oncol 2012; 13(5): 518-27.
69. Macdonald S. Aspirin use to be banned in under 16 year olds. BMJ 2002; 325(7371): 988.
70. Schrör K. Aspirin and Reye syndrome: a review of the evidence. Paediatr Drugs 2007; 9(3): 195-204.
71. Pugliese A, Beltramo T, Torre D. Reye's and Reye's-like syndromes. Cell Biochem Funct 2008; 26(7): 741-6.
72. Hurwitz ES. Reye's syndrome. Epidemiol Rev 1989; 11: 249-53.
73. Meremikwu MM, Okomo U. Sickle cell disease. BMJ Clin Evid 2011; 2011: 2402.
74. Mohamed S, Fong CM, Ming YJ, Kori AN, Wahab SA, Ali ZM. Evaluation of an initiation regimen of warfarin for international normalized ratio target 2.0 to 3.0. J Pharm Technol 2021; 37(6): 286-92.
75. Chu MWA, Ruel M, Graeve A, Gerdisch MW, Ralph J, Damiano Jr RJ, Smith RL. Low-dose vs standard warfarin after mechanical mitral valve replacement: A randomized trial. Ann Thorac Surg 2023; 115(4): 929-38.
76. Crowther MA, Douketis JD, Schnurr T, Steidl L, Mera V, Ultori C, et al. Oral vitamin K lowers the international normalized ratio more rapidly than subcutaneously vitamin K in the treatment of warfarin-associated coagulopathy. A randomized, controlled trial. Ann Intern Med 2002; 137(4): 251-4.
77. Brown DG, Wilkerson EC, Love WE. A review of traditional and novel oral anticoagulant and antiplatelet therapy for dermatologists and dermatologic surgeons. J Am Acad Dermatol 2015; 72(3): 524-34.
78. Delaney JA, Opatrny L, Brophy JM, Suissa S. Drug drug interactions between antithrombotic medications and the risk of gastrointestinal bleeding. CMAJ 2007; 177(4): 347-51.
79. Dahal K, Kunwar S, Rijal J, Schulman P, Lee J. Stroke, major bleeding, and mortality outcomes in warfarin users with atrial fibrillation and chronic kidney disease: a meta-analysis of observational studies. Chest 2016; 149(4): 951-9.
80. Chai-Adisaksopha C, Lorio A, Hillis C, Siegal D, Witt DM, Schulman S, et al. Warfarin resumption following anticoagulant-associated intracranial hemorrhage: A systematic review and meta-analysis. Thromb Res 2017; 160: 97-104.
81. Ferro JM, Coutinho JM, Dentali F, Kobayashi A, Alasheev A, Canhao P, et al. Safety and efficacy of dabigatran etexilate vs dose-adjusted warfarin in patients with cerebral venous thrombosis: A randomized clinical trial. JAMA Neurol 2019; 76(12): 1457-65.
82. Meade TW. Low-dose warfarin and low-dose aspirin in the primary prevention of ischemic heart disease. Am J Cardiol 1990; 65(6): 7C-11C.
83. Singer DE, Hughes RA, Gress DR, Sheehan MA, Oertel LB, Maraventano SW, et al. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. N Engl J Med 1990; 323(22): 1505-11.
84. Levine M, Hirsh J, Gent M, Arnold A, Warr D, Falanya A, et al. Double-blind randomised trial of a very-low-dose warfarin for prevention of thromboembolism in stage IV breast cancer. Lancet 1994; 343(8902): 886-9.
85. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014; 383(9921): 955-62.
86. Vinogradova Y, Coupland C, Hill T, Hippisley-Cox J. Risks and benefits of direct oral anticoagulants versus warfarin in a real world setting: cohort study in primary care. BMJ 2018; 362: k2505.
87. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009; 361(12): 1139-51.
88. Helvaci MR, Cayir S, Halici H, Sevinc A, Camci C, Abyad A, Pocock L. Terminal endpoints of systemic atherosclerotic processes in sickle cell diseases. World Family Med 2024; 22(5): 13-23.
89. Helvaci MR, Daglioglu MC, Halici H, Sevinc A, Camci C, Abyad A, Pocock L. Low-dose aspirin plus low-dose warfarin may be the standard treatment regimen in Buerger's disease. World Family Med 2024; 22(6): 22-35.
90. Helvaci MR, Erden ES, Aydin LY. Atherosclerotic background of chronic obstructive pulmonary disease in sickle cell patients. HealthMED 2013; 7(2): 484-8.
91. Rennard SI, Drummond MB. Early chronic obstructive pulmonary disease: definition, assessment, and prevention. Lancet 2015; 385(9979): 1778-88.
92. Schoepf D, Heun R. Alcohol dependence and physical comorbidity: Increased prevalence but reduced relevance of individual comorbidities for hospital-based mortality during a 12.5-year observation period in general hospital admissions in urban North-West England. Eur Psychiatry 2015; 30(4): 459-68.
93. Singh G, Zhang W, Kuo YF, Sharma G. Association of Psychological Disorders With 30-Day Readmission Rates in Patients With COPD. Chest 2016; 149(4): 905-15.
94. Mannino DM, Watt G, Hole D, Gillis C, Hart C, McConnachie A, et al. The natural history of chronic obstructive pulmonary disease. Eur Respir J 2006; 27(3): 627-43.
95. Mapel DW, Hurley JS, Frost FJ, Petersen HV, Picchi MA, Coultas DB. Health care utilization in chronic obstructive pulmonary disease. A case-control study in a health maintenance organization. Arch Intern Med 2000; 160(17): 2653-58.

96. Anthonisen NR, Connett JE, Enright PL, Manfreda J; Lung Health Study Research Group. Hospitalizations and mortality in the Lung Health Study. Am J Respir Crit Care Med 2002; 166(3): 333-9.
97. McGarvey LP, John M, Anderson JA, Zvarich M, Wise RA; TORCH Clinical Endpoint Committee. Ascertainment of cause-specific mortality in COPD: operations of the TORCH Clinical Endpoint Committee. Thorax 2007; 62(5): 411-5.
98. Trent JT, Kirsner RS. Leg ulcers in sickle cell disease. Adv Skin Wound Care 2004: 17(8); 410-6.
99. Minniti CP, Eckman J, Sebastiani P, Steinberg MH, Ballas SK. Leg ulcers in sickle cell disease. Am J Hematol 2010; 85(10): 831-3.
100. Yawn BP, Buchanan GR, Afenyi-Annan AN, Ballas SK, Hassell KL, James AH, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014; 312(10): 1033-48.
101. Helvaci MR, Aydogan F, Sevinc A, Camci C, Dilek I. Platelet and white blood cell counts in severity of sickle cell diseases. HealthMED 2014; 8(4): 477-82.
102. Myers KA, Farquhar DR. The rational clinical examination. Does this patient have clubbing? JAMA 2001; 286(3): 341-7.
103. Toovey OT, Eisenhauer HJ. A new hypothesis on the mechanism of digital clubbing secondary to pulmonary pathologies. Med Hypotheses 2010; 75(6): 511-3.
104. Nassiri AA, Hakemi MS, Asadzadeh R, Faizei AM, Alatab S, Miri R, et al. Differences in cardiovascular disease risk factors associated with maximum and mean carotid intima-media thickness among hemodialysis patients. Iran J Kidney Dis 2012; 6(3): 203-8.
105. Helvaci MR, Gokce C, Sahan M, Hakimoglu S, Coskun M, Gozukara KH. Venous involvement in sickle cell diseases. Int J Clin Exp Med 2016; 9(6): 11950-7.
106. Xia M, Guerra N, Sukhova GK, Yang K, Miller CK, Shi GP, et al. Immune activation resulting from NKG2D/ligand interaction promotes atherosclerosis. Circulation 2011; 124(25): 2933-43.
107. Hall JE, Henegar JR, Dwyer TM, Liu J, da Silva AA, Kuo JJ, et al. Is obesity a major cause of chronic kidney disease? Adv Ren Replace Ther 2004; 11(1): 41-54.
108. Nerpin E, Ingelsson E, Risérus U, Helmersson-Karlqvist J, Sundström J, Jobs E, et al. Association between glomerular filtration rate and endothelial function in an elderly community cohort. Atherosclerosis 2012; 224(1): 242-6.
109. Stengel B, Tarver-Carr ME, Powe NR, Eberhardt MS, Brancati FL. Lifestyle factors, obesity and the risk of chronic kidney disease. Epidemiology 2003; 14(4): 479-87.
110. Bonora E, Targher G. Increased risk of cardiovascular disease and chronic kidney disease in NAFLD. Nat Rev Gastroenterol Hepatol 2012; 9(7): 372-81.
111. Helvaci MR, Cayir S, Halici H, Sevinc A, Camci C, Sencan H, Davran R, Abyad A, Pocock L. Acute chest syndrome and coronavirus disease may actually be genetically determined exaggerated immune response syndromes particularly in pulmonary capillaries. World Family Med 2024; 22(3): 6-16.
112. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, et al. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol 2006; 17(7): 2034-47.
113. Helvaci MR, Aydin Y, Aydin LY. Atherosclerotic background of chronic kidney disease in sickle cell patients. HealthMED 2013; 7(9): 2532-7.
114. DeBaun MR, Gordon M, McKinstry RC, Noetzel MJ, White DA, Sarnaik SA, et al. Controlled trial of transfusions for silent cerebral infarcts in sickle cell anemia. N Engl J Med 2014; 371(8): 699-710.
115. Majumdar S, Miller M, Khan M, Gordon C, Forsythe A, Smith MG, et al. Outcome of overt stroke in sickle cell anaemia, a single institution's experience. Br J Haematol 2014; 165(5): 707-13.
116. Kossorotoff M, Grevent D, de Montalembert M. Cerebral vasculopathy in pediatric sickle-cell anemia. Arch Pediatr 2014; 21(4): 404-14.
117. Charache S, Terrin ML, Moore RD, Dover GJ, Barton FB, Eckert SV, et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. N Engl J Med 1995; 332(20): 1317-22.

Evaluating the Impact of Green Prescribing on Respiratory Disease Control: A Quality Improvement Project

Amjad Abdelmageed[1], Mohamed Elhimadie[2] , Ahmed Abdalla[3]

(1) MBBS, MRCGP, PGDIP Research Methodology & Biostatistics
(2) MBBS, MRCGP, PGDIP MSK & Rheumatology Plymouth University
(3) MBBS

Corresponding author :
Dr. Mohamed Elhimadie
Email: mo_special@hotmail.com

Received: April 2025. Accepted: May 2025; Published:June 1, 2025.
Citation: Amjad Abdelmageed, Mohamed Elhimadie, Ahmed Abdalla Moh. Evaluating the Impact of Green Prescribing on Respiratory Disease Control: A Quality Improvement Project. World Family Medicine. June 2025; 23(4): 54 - 56. DOI: 10.5742/MEWFM.2025.795257870

Abstract

Green prescribing promotes environmentally sustainable healthcare by encouraging the use of lower-carbon alternatives, such as dry powder inhalers (DPIs) in place of metered-dose inhalers (MDIs). This quality improvement project evaluated disease control in 54 patients with asthma or COPD who were switched from MDIs to DPIs as part of routine care.

Keywords: green prescribing, respiratory disease control, quality improvement

Introduction

Green prescribing involves selecting and prescribing medications or medical devices that have a lower environmental impact while ensuring effective patient care. This practice is part of sustainable healthcare efforts to reduce the carbon footprint of the healthcare sector, particularly in areas like pharmaceuticals and medical devices.

It is important to distinguish the focus of this investigation, the impact of selecting medications or medical devices based on their carbon footprint and environmental impact, from green social prescribing, which involves healthcare professionals recommending non-clinical, nature-based interventions such as exercise, dietary changes, mindfulness sessions, and social or environmental activities.

Green prescribing typically includes, but is not limited to, promoting reusable or recyclable medical devices to minimize waste (1) and prioritizing medications that require less energy-intensive production processes or generate less waste throughout their lifecycle (2). One example is switching patients to environmentally friendly inhalers, such as dry powder inhalers (DPIs) or soft mist inhalers (SMIs), which do not rely on hydrofluorocarbon (HFC) propellants (3,4). These inhalers have a significantly lower carbon footprint compared to traditional metered-dose inhalers (MDIs), which use HFC propellants, potent greenhouse gases. (5) Green prescribing would also involve avoiding overprescription and promoting evidence-based use of medications to prevent unnecessary production and disposal of pharmaceuticals (6).

Methodology

This small-scale quality improvement project (QIP) investigates the impact of switching patients with respiratory conditions, such as asthma and chronic obstructive pulmonary disease (COPD), to environmentally friendly inhalers for disease control.

We conducted a retrospective observational analysis of a cohort of patients who had previously switched from traditional MDIs to DPIs. Their asthma or COPD was evaluated by comparing clinical data before and after the transition to assess any variation in disease control.

Result

A total of 54 patients with asthma or chronic obstructive pulmonary disease (COPD) who had previously been using a metered-dose inhaler (MDI) and were subsequently switched to a dry powder inhaler (DPI) as part of routine clinical care, were included. The aim was to assess changes in disease control before and after the switch.
Among the 54 patients; 31 patients (57.4%) showed no change in disease control following the switch to DPI, indicating that the DPI was similarly effective to the MDI in these cases.18 patients (33.3%) demonstrated a subjective improvement in disease control after the change. 4 patients (7.4%) were reverted back to MDI due to difficulties using the DPI device, primarily related to inadequate inspiratory effort. 1 patient (1.9%) experienced worsening of disease control after the change to DPI and was also switched back to MDI.

Overall, 49 out of 54 patients (90.7%) either experienced stable or improved disease control following the inhaler switch.

Discussion

The industrialized healthcare sector is estimated to contribute approximately 4%–5% of global greenhouse gas (GHG) emissions (7). The carbon footprint of a commonly prescribed metered-dose inhaler (MDI), such as salbutamol, is estimated to be equivalent to driving a mid-sized family car for approximately 175 miles (per inhaler), whereas the equivalent dry powder inhaler (DPI) produces emissions comparable to driving only 4 miles (8).

The findings of this small study align with existing evidence in the literature, indicating that dry powder inhalers (DPIs) are as clinically effective as metered-dose inhalers (MDIs) in managing respiratory conditions (9). As such, DPIs present a viable alternative to MDIs due to their substantially lower carbon footprint while maintaining similar clinical efficacy (10.11).

Most patients can use a DPI effectively. However, certain patients may find it difficult to use a DPI, as it requires sufficient negative inspiratory pressure to function properly. This means that individuals, such as children or those with significantly compromised lung function, may not be able to use a DPI. Patient selection is therefore crucial, and it is important to ensure that patients have adequate respiratory effort using inhaler checking devices.

Additionally, patient choice would also play a major role here. Surveys indicate that patients are concerned about the environmental impact of healthcare and are generally receptive to switching their inhaler based on this (12,13). However there is also evidence suggesting that patients believe environmental factors should not influence their treatment decisions (14). Healthcare providers can support patients in selecting the most suitable inhaler by utilizing tools such as the NICE patient decision aid on inhalers and climate change (15).

One of the main challenges of green prescribing is the higher cost of greener alternatives, however, accepting these small increased costs is necessary, as the long-term environmental benefits, such as mitigating climate change, can outweigh the immediate financial impact. Another challenge is the limited awareness among healthcare professionals and patients about the environmental impact of medications and devices, highlighting the need for better education on the importance of sustainable green prescribing.

Conclusion

Green prescribing aligns with global efforts to combat climate change, offering sustainable and environmentally friendly options for maintaining high standards of patient care. It is an evolving area of healthcare that emphasizes the responsible use of resources and prescribing practices, contributing to a healthier planet and population.

We advocate for the adoption of a policy on environmental prescribing to standardize decision-making across clinical settings, thereby amplifying its impact. Healthcare has a responsibility to be environmentally sustainable, and consensus-based prescribing can play a key role in achieving this goal.

References

1. British Thoracic Society. Guidelines for the management of asthma. Thorax. 2022;77(1):1-45.
2. National Institute for Health and Care Excellence (NICE). Asthma: Diagnosis, Monitoring, and Chronic Asthma Management [NG80]. London: NICE; 2017 [updated 2020].
3. Janson C, Henderson R, Löfdahl M, Hedberg M, Sharma R, Wilkinson A. The environmental impact of inhaler use in Europe and how to reduce it. Eur Respir J. 2020;55(2):1901598.
4. NHS England. Delivering a 'Net Zero' National Health Service. NHS Long Term Plan. 2020. Available from: https://www.england.nhs.uk/greenernhs/
5. Wilkinson A, Woodcock J, Smith R. Carbon footprint of inhalers: A UK-based study. BMJ Open. 2019;9(10):e028763.
6. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2023. Available from: https://goldcopd.org/
7. Sustainable Development Unit. Reducing the use of natural resources in health and social care [Internet]. 2018. Available from: https://networks.sustainablehealthcare.org.uk/sites/default/files/resources/20180912_Health_and_Social_Care_NRF_web.pdf
8. Green Inhaler. Green inhalers. Available from: https://greeninhaler.org
9. Parker J. DPIs and MDIs: comparing clinical effectiveness in managing respiratory disease. J Med Ethics. 2023;49(1):92–8. doi:10.1136/medethics-2022-108388.
10. Janson C, Henderson R, Löfdahl M, et al. Carbon footprint impact of the choice of inhalers for asthma and COPD. Thorax. 2020;75(1):82–4.
11. Wilkinson A, Woodcock A. The environmental impact of inhalers for asthma: a green challenge and a golden opportunity. Br J Clin Pharmacol. 2022;88(7):3016–22.
12. Liew K, Wilkinson A. P280 How do we choose inhalers? Patient and physician perspectives on environmental, financial, and ease-of-use factors. Thorax. 2017;72:A235-7.
13. D'Ancona G, Cumella A, Renwick C. The sustainability agenda and inhaled therapy: what do patients want? Eur Respir J. 2021;58(suppl 65):PA3399.
14. The Health Foundation. Going green: what do the public think about the NHS and climate change? 2021. Available from: https://www.health.org.uk/publications/long-reads/going-green-what-do-the-public-think-about-the-nhs-and-climate-change.
15. National Institute for Health and Care Excellence (NICE). BTS, NICE and SIGN patient decision aid on asthma inhalers and climate change [Internet]. London: NICE; 2021 Available from: https://www.nice.org.uk/guidance/ng245/resources/bts-nice-and-sign-patient-decision-aid-on-asthma-inhalers-and-climate-change-pdf-13558151917

The Pattern of Gynecological Malignancies in Hadhramout Governorate, Yemen: An Overview of 10 Years

Laila Mohammed Bamatraf[1], Fauzia Faraj Bamatraf [2], Abdullah Mubarak Kaity [3]

(1) Assistant Professor of Family Planning and Reproductive Health, Medical Fundamental Department, College of Nursing. Hadhramout University,
Republic of Yemen
(2) MD, MSc, Professor of Community Health, Department of Community Medicine College of Medicine and Health Sciences, Hadhramout University (HUCOM),
Republic of Yemen
(3) Assistant Professor of Public Health, Medical Fundamental Department, College of Nursing. Hadhramout University, Republic of Yemen

Corresponding author:
Prof Dr. Fauzia F Bamatraf MD, MSc,
Professor of Community Health.
Department of Community Medicine College of Medicine and Health Sciences, Hadhramout University (HUCOM), Republic of Yemen
Mobile: +967 735306070
Email: ffbamatraf2008@yahoo.com

Received: April 2025. Accepted: May 2025; Published:June 1, 2025.
Citation: Laila Mohammed Bamatraf, Fauzia Faraj Bamatraf, Abdullah Mubarak Kaity. The Pattern of Gynecological Malignancies in Hadhramout Governorate, Yemen: An Overview of 10 Years. World Family Medicine. June 2025; 23(4): 57 - 65.
DOI: 10.5742/MEWFM.2025.795257871

Abstract

Background: Gynecological cancer is a leading cause of cancer-related deaths worldwide, with its prevalence and incidence varying from region to region. It's incidence and mortality can affect women's quality of life and increase the healthcare burden on healthcare institutions worldwide. This study aimed to determine the pattern, distribution, and trends of gynecological malignancies at the Hadhramout National Oncology Center (HNOC), Yemen, over a ten-year period.

Methods: This retrospective descriptive study was conducted in Hadhramout Governorate, eastern Yemen, and relied on data collected from the medical records of all gynecological malignancies registered at the HNOC during the study period from January 1, 2014, to December 31, 2023. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 20, and percentages and frequencies are presented.

Results: This study included 326 cases with histologically confirmed gynecological malignancies. The study results showed that ovarian cancer (40.2%) was the most common cancer type, followed by cervical cancer (33.4%) and uterine cancer (19.6%). Choriocarcinoma (3.7%) was the least common, followed by vaginal cancer (2.5%) and vulvar cancer (0.6%). Cervical and Choriocarcinoma cancers were most prevalent among younger women (aged 30–39 and 21–29, respectively). In the case of ovarian cancer, the majority of patients were diagnosed between the ages of 50 and 59, while uterine, vaginal, and vulvar cancers occurred in older patients (>60 years). Trends in all gynecological cancers registered at HNOC showed an increase over the study period.

Conclusion: The most common gynecological malignancies are ovarian, cervical, and uterine cancer, and the number of gynecological cancer cases registered at HNOC is increasing. There is a need to increase public awareness, especially among young women, about screening and vaccination programs.

Keywords: Gynecological Malignancies, Hadhramout Governorate, Yemen.

Introduction

Cancer remains one of the major health concerns globally, with an estimated 19.3 million new cancer cases (18.1 million excluding non-melanoma skin cancer) and nearly 10 million cancer deaths (9.9 million excluding non-melanoma skin cancer) occurring in 2020 worldwide [1]. Cancer has been found to increase with lifestyle behaviors such as poor dietary habits, smoking, reproductive characteristics including low birth rate, first birth at advanced age, etc., which has led to an increased cancer burden in developing countries [2].

Gynecological cancer is also a concern regarding women's overall health. Gynecological cancer is a leading cause of cancer-related deaths worldwide, with its prevalence and incidence varying from region to region [3]. The comprehensive global cancer statistics from the International Agency for Research on Cancer indicate that gynecological cancers accounted for 20% of the estimated 14.1 million new cancer cases and 8.2 million cancer deaths among women worldwide in 2022 [3]. Gynecologic malignancies include cancer of the ovary, fallopian tube, uterus (body of the uterus), cervix, vagina, and vulva, as well as choriocarcinoma (carcinoma of the placenta). The pattern of gynecologic malignancies varies across geographic regions due to differences in environment, lifestyle, genetic makeup, and socioeconomic background [4].

Globally, cervical cancer is the fourth most common cancer among women and fifteenth among all cancers with approximately 660,000 new cases reported in 2022. In the same year, approximately 94% of the 350,000 cervical cancer deaths occurred in low- and middle-income countries [5,6]. The highest cervical cancer incidence and mortality rates are found in sub-Saharan Africa, Central America, and Southeast Asia [7]. Regional variations in the burden of cervical cancer are linked to unequal access to vaccination, screening, and treatment services [8].

Ovarian cancer is considered a silent killer. It has the highest mortality rate in developing countries as two-thirds of the cases present at an advanced stage [9]. The main risk factors for ovarian cancer increase with age, family history of breast, ovarian, uterine, and colon cancer, use of fertility drugs, and infertility [10]. There are more than 204,000 new cases of ovarian cancer annually worldwide, including about 43,000 new cases in the UK and 22,000 cases in the United States [11].

Endometrial cancer is the most common cancer of the female reproductive system, the fourth most common cancer among women in the United States, and the fifth most common cause of cancer among women worldwide [12,13]. Reports indicate that the incidence of endometrial cancer is higher in more developed countries and lower in Africa and Asia. Although the incidence rate is still higher in these countries, the global incidence of this malignancy has increased by more than 130% over the past 30 years [14]. Endometrial cancer primarily affects postmenopausal women, with a peak incidence between the ages of 55 and 65, while ovarian cancer is most common between the ages of 45 and 65. Cervical cancer peaks at age 45 [15,16].

Vaginal and vulvar cancers are rare, accounting for approximately 2% and 3% of gynecological cancers, respectively. This disease primarily affects women over the age of 60. Choriocarcinoma is a type of gestational trophoblastic disease, with the highest incidence observed among younger women between the ages of 21-39, with most cases being associated with pregnancy [17].

In Arab countries, breast cancer is the most common cancer among women, followed by cervical cancer. Ovarian cancer is the fourth most common cancer among women. Available resources vary widely across Arab countries. However, challenges to providing gynecological cancer services are similar, such as cultural and religious backgrounds. Most gynecological cancers are diagnosed at a late stage in Arab countries due to a lack of awareness about reproductive health, especially among older women, as well as the cultural stigma associated with seeking medical advice for gynecological symptoms [18]. Arab countries are projected to see an increase in cancer incidence and mortality; however, there are limited studies comparing cancer epidemiology in Arab countries with other parts of the world [18].

Limited information is available on gynecological malignancies in Yemen. To our knowledge, this is the first study conducted in eastern Yemen, specifically in Hadhramout Governorate. Therefore, this study was conducted to determine the pattern, distribution, and trends of gynecological malignancies at the Hadhramout National Oncology Center (HNOC) in Hadhramout Governorate, Yemen, during the period from January 1, 2014, to December 31, 2023.

Materials and Methods

This retrospective descriptive study was conducted in Hadhramout Governorate, eastern Yemen, and relied on data collected from medical records. The medical records of all patients registered at the Hadhramout National Oncology Center (HNOC) during the study period were reviewed to identify patients with gynecological malignancies. The study covered a ten-year period from January 1, 2014, to December 31, 2023. Cases with confirmed histological diagnosis were included. Cases from other governorates were excluded. Of the total collected cases (390), 64 were removed, resulting in a final count of 326. Data were coded and reviewed. Patient sex, age, diagnosis, tumor site, year of incidence, and place of residence (governorate) were entered using the Statistical Package for the Social Sciences (SPSS) version 20. Data were analyzed using percentages and frequencies. We obtained ethical approval for the study from the Ethics and Research Review Committee of the College of Nursing and the College of Medicine and Health Sciences at Hadhramout University. We also obtained a letter from the Colleges to the Director of the Hadhramout National

Oncology Center to facilitate our study. Patient information was collected using a form. The records were treated confidentially. The patient's name, file number, or any personal information was not included. The researchers kept the data sheet in a private file.

Results

A total of 326 cases with histologically confirmed diagnoses of gynecological malignance were included in this study. The results of the study showed that the patients' ages ranged from 11 to 90 years. The mean of their age was 51.43 ± 15.50 years (Table 1).

As shown in Table 2 ovarian and cervical cancer were the most common among the study sample, followed by uterine cancer (40.2%, 33.4%, and 19.6%, respectively). Table 2 also shows that the least common cancer was choriocarcinoma (3.7%), followed by vaginal cancer (2.5%) and vulvar cancer (0.6%).

Regarding the distribution of gynecological malignancies by patient age Table 3 shows that ovarian cancers (58.0%) were more common among women aged 50-59 while cervical cancer was most common (42.2%) among young women aged 30-39 Uterine cancer was more common (67.2%) among women in the older age group of 60-69 years. The same table also shows that almost all cases of vaginal and vulval cancers (100%) occurred in women over the age of 70 years, while Choriocarcinoma occurred primarily among younger women in age group (21-29) and (30–39) years.

Regarding the trend of gynecological cancer registered in HNOC over a period of ten years from 2014 to 2023, Table 4 shows the cancer cases increasing from 7.1% in year 2015 to 10.4% and 11.3% in years 2016 and 2017 respectively, then decreasing to 9.2%, 8.9%, 8.0% and 7.1% in the next four years from 2019 to year 2021 respectively. Then the increase was also recorded in 2022 to 13.5%, and the largest increase occurred in 2023, reaching 16.6%.

Table 1: Distribution of patients by age group

Age group of patients (years)	Frequency	%
20 and less	11	3.4
21 to 29 years	18	5.5
30-39 years	46	14.1
40 to 49 years	58	17.8
50 to 59 years	76	23.3
60 to 69 years	74	22.7
70 years & above	43	13.2
Mean ± SD	51.43 ± 15.50	

Table 2. Site distribution of gynecological malignancies (N=326)

Site of malignancy	Frequency	%
Ovarian cancer	131	40.2
Cervical cancer	109	33.4
Uterine cancer	64	19.6
Choriocarcinoma	12	3.7
Vaginal cancer	8	2.5
Vulvar cancer	2	0.6
Total	326	100.0

Table 3. Distribution of gynecological malignancies according to age of patient (N= 326

Age group (years)	Site of cancer					
	Ovary N %*	Cervix N %*	Uterine N %*	Vagina N %*	Choriocarcinoma N %*	Vulva N %*
20 and less	0 (0.0%)	11 (10.1%_	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
21-29	0 (0.0%)	18(16.5%)	0 (0.0%)	0 (0.0%)	4 (33.3%)	0 (0.0%)
30-39	0 (0.0%)	46 (42.2%)	0 (0.0%)	0 (0.0%)	5 (41.7%)	0 (0.0%)
40 to 49	24 (18.3%)	24 (18.3%)	0 (0.0%)	0 (0.0%)	2 (16.7%)	0 (0.0%)
50 to 59	76 (58.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (8.3%)	0 (0.0%)
60 to 69	31 (23.7%)	19 (14.5%)	43 (67.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
70 ≥	0 (0.0%)	0 (0.0%)	21(32.8%)	8 (100.0%)	0 (0.0%)	2 (100.0%)
Total	109 100.0%	131 100.0%	64 100.0%	8 100.0%	12 100.0%	2 100.0%

* Number and percentage

Table 4: Percent distribution and trend of gynecological cancer registered in HNOC over the period 2014-2023

Year	Number of cases	Percentages
2014	25	7.7
2015	23	7.1
2016	35	10.7
2017	37	11.3
2018	30	9.2
2019	29	8.9
2020	26	8.0
2021	23	7.1
2022	44	13.5
2023	54	16.6
Total	326	100.0

Discussion

Cancer ranks as a leading cause of death and an important barrier to increasing life expectancy in every country of the world [19]. Gynecological cancers are a leading cause of cancer-related deaths worldwide [3]. Their high incidence and mortality rates can impact women's quality of life and increase the healthcare burden on healthcare institutions worldwide [20].

Our study revealed that ovarian cancer was the first most common cancer, accounting for 40.2% of all gynecological malignancies, which is comparable to the results of the previous study conducted by Jamal et al. among Yemeni women registered and treated at the National Oncology Center in Aden Governorate [21]. Also this observation is consistent with the results of studies conducted in Libya by Ibrahim et al. [22], in Pakistan by Nabila et al. [23], in Ethiopia by Himanot et al. [24], and in Nepal by Bishal [25], where ovarian cancer was found to be the most common cancer in their findings. Ovarian cancer is also more common in developed countries, especially in North America and Europe [26]. This may be attributed to new lifestyle trends, which are contributing factors, such as delayed pregnancy, short family duration, and limited breastfeeding [27]. Contrary to our findings, the results of a study conducted by Fram et al. in Jordan indicated that ovarian cancer ranked second among Jordanian women [28] while a study conducted by Hamed et al in the United Arab Emirates (UAE) indicated that ovarian cancer ranked third among all women in the UAE [29]. It is worth noting that the pattern of gynecological malignancies varies across geographic regions due to differences in environment, lifestyle, genetic makeup, and socioeconomic background [4]. Furthermore, the high incidence of ovarian cancer in our study and other studies conducted in developing countries may be attributed to changes in the dietary habits of the population of these countries, including Yemen, over the past decade, which, along with decreased physical activity, has contributed to weight gain in women. Obesity is clearly associated with higher rates of ovarian cancer [30].

Our study demonstrated that, cervical cancer is ranked the second most common cancer of all gynecological malignancies. This finding is in agreement with the results of the previous study conducted by Jamal et al. among Yemeni women in Aden governorate [21], as well as is consistent with those reported in other countries in which cervical cancer was the second most common cancer of all gynecological malignancies [22,23,24,25]. On the other hand, our results were in contrast with published data from other Arab and developing countries including Saudi Arabia, Bangladesh, India and Nigeria [31,32,33,34], which reported that cervical cancer was the most common cancer accounting for the largest number of gynecological cases, followed by ovarian and uterine cancer.

It is clear from the above that numerous studies conducted in developing countries have reported that cervical cancer is the most common malignant tumor of the reproductive organs. However, cervical cancer has been found to have the highest incidence and mortality rates worldwide [5,6]. It is not surprising to know that cervical cancer is a preventable disease thanks to the availability of effective and widespread screening programs, a long pre-operative period, and effective treatment. However, overall, the high incidence rate, especially in developing countries, reflects the weakness of screening programs for early detection of precancerous conditions [35]. In contrast, the presence of widespread cervical screening programs in the developed world has significantly reduced the burden of cervical malignancies.

Uterine cancer was the third most common gynecological malignancy among our study patients, which is similar to the results of a previous study by Jamal et al. among Yemeni women in Aden Governorate [21] and to the results from other developing countries which reported that uterine cancer was the third most common gynecological malignancy [36,37,38]. However, the incidence of endometrium cancer is higher in developed countries and lower in Africa and Asia [14]. On the other hand in contrast to our results, studies conducted in Arab countries, such as Hamed's study in the United Arab Emirates [29], Nawal Al-Mohammadi's study in Al-Madinah Al-Munawarah [39], and Faramin's study in Jordan [28], reported that uterine cancer ranked first among gynecological malignancies among their study patients. Furthermore, results from other studies by Sahar Rostami et al. in Iran and Nasreen in Pakistan reported that uterine cancer ranked second among gynecological cancers among their study patients [40,41]. It should be noted that the pattern and incidence rates of gynecological malignancies in this study and the results of other studies conducted in Arab countries and other parts of developing countries vary, possibly due to differences in environment, lifestyle, genotype, and socioeconomic background from one region to another [18].

The current study shows that the ages of patients ranged from 11 to 90 years, with a mean of 51.43 ± 15.50 years, which is comparable to the mean ages of gynecological patients in other studies [42,43]. A review on menopause and gynecological malignancy supported these results, stating that the probability of developing genital tract-related cancers generally increased with the woman's age [44].

Regarding the age of patients at the time of diagnosis of gynecological malignancies, our study showed that ovarian cancer was most common among patients aged 50–59 years. Similar findings have been found in other developing and developed countries. These studies were conducted in Nigeria, Pakistan, Jordan and the United Arab Emirates [34,36,28,29]. Additionally, our findings are supported by the results of a study conducted in the United Kingdom [45], which showed that ovarian cancer was most common in the fifth and sixth decades of life.

However, our findings contradict the results of a study conducted by Nawal Al-Mohammadi in Al-Madinah Al-Munawarah region, Saudi Arabia, which indicated that ovarian cancer was most common in the age group of 30 years and younger [38]. On the other hand, a previous study conducted in Yemen [21] and other developing countries showed that these malignancies were most common in the age group of 40–49 years [32, 46]. Meanwhile, the results of a study conducted by Okunade et al. in Nigeria [47] and in India by Choudhary et al. [33] indicated that the highest incidence of malignant ovarian cancer occurred in the age group of 60 to 70 years. Ovarian cancer is one of the most common gynecological cancers, with the highest mortality rate in both developed and developing countries [48]. Late-stage diagnosis requires long, complex, aggressive, and expensive treatment; therefore, the management of ovarian cancer in developing countries is a major challenge (48).

Regarding cervical cancer, our results revealed that cervical cancer is more prevalent among younger women (30–39 years old). Incidence rates among younger generations have also been reported from neighboring Arab countries, such as the United Arab Emirates and Al-Madinah Al-Munawarah region, Saudi Arabia, where cervical cancer was more common among women in their 30s and 40s [29,39]. In contrast to our results, the incidence of cervical cancer at symptom onset among Yemeni women in a previous study [21] was observed in the 40–49 age group. Stewart et al [49], reported a similar finding in the 45–49 age group, while Haimanot et al in Ethiopia [24] reported that, the incidence rate was in the 40–49 age group. On the other hand, the median age at symptom onset of cervical cancer in the Indian study [37] was 50 years, which is close to the median age reported by the Surveillance, Epidemiology, and End Results (SEER) program (in the United States) and the European Union [50,51].

On the other hand, studies conducted in Nigeria and Jordan reported that cervical cancer is more prevalent among older women aged 50-60 years [2834]. Cervical cancer has been found to have the highest prevalence and mortality rates worldwide, but it is a preventable disease through effective and widespread screening programs, a long pre-invasive period, and effective treatment [52].

The study showed that, uterine cancer is the third most common malignant tumor of the female reproductive system, with the majority of patients (96.9%) presenting in the older age group (61–70 years). This is consistent with the findings in other studies from the United Arab Emirates, Bangladesh, India, Pakistan, Nigeria and Botswana [29,32,37,46,47,53]. In Western countries, particularly the United States, endometrial cancer is the fourth most common type of female reproductive cancer, primarily affecting postmenopausal women, with a median age of 60. It is rare in women under 45 years old [54]. Globally, the incidence of endometrial cancer peaks between the ages of 65 and 75 [55].

The current study shows that choriocarcinoma (3.7%) is the fourth most common gynecological malignancy, with a higher prevalence among younger women (30-39 years and 21-29 years, respectively) and most cases are associated with pregnancy. Findings from other developing countries have indicated that this disease is more common among women of reproductive age (34-45), which is comparable to the results of the current study, as well as to those of a previous study in Yemen [21]. The incidence of this disease in Yemen may be related to low socioeconomic status and poor education. Previously published data have indicated that the highest incidence rate in Asia is generally attributed to low socioeconomic status and poverty [56]. As noted in our study and others, choriocarcinoma is a disease that affects relatively younger women, perhaps because the disease is associated with pregnancy and, therefore, is more likely to occur in women with an active reproductive life.

Vaginal and vulvar cancer were the least common gynecological malignancy in this study, accounting for only (2.5% and 0.6% respectively) of female genital cancers, with a common age group (≥ 70 years). This finding is consistent with other studies conducted in developing countries, which reported that vulvar and vaginal cancers are more common in women over the age of 60. A study conducted in Saudi Arabia indicated that these malignancies are more common in women over the age of 75 [39], and in Nigeria and Botswana, cases were recorded in women over the age of 70 [34,53], while in Bangladesh and Pakistan, it was more common in women over the age of 60 [32,46]. Various studies have shown a decrease in the incidence of vulvar and vaginal malignancies, and this rate does not change significantly over time [57,58,59].

Regarding the trend in gynecological malignancies in this study, the incidence of gynecological cancers was found to have increased overall over the ten-year study period. Notably, the trends in the incidence of gynecological cancers in our study area are similar to those observed in Arab and developing countries [18,60,61]. There is a high incidence and mortality rate from gynecological cancers in developing countries in general, primarily due to the failure of these countries to implement effective national screening and vaccination programs [62].

Conclusion and Recommendations

In conclusion the study showed that, the number of patients with gynecological cancers presenting to the HNOC is steadily increasing. Ovarian cancer was the most common cancer followed by cervical and uterine cancers. There is a need to increase public awareness, particularly among young women, about screening programs, vaccination, and early referral to a doctor when symptoms and warning signs appear, to prevent, diagnose, and treat the disease early and appropriately. Further studies should be conducted to identify potential risk factors for these cancers among women, determine trends over time, and project the scope of the cancer problem in the future.

This information may help in developing a cancer control plan and targeted interventions to prevent gynecological cancers, especially in the study area and in Yemen in general.

Limitation

To our knowledge, this is the first study of its kind to identify the patterns, distribution, and trends of gynecological cancers in Hadhramout Governorate, Yemen. This study was hindered by some unavoidable limitations. The retrospective study design relied on previously collected data, and information on some important variables including tumor stage and other demographic variables, was missing because they were not recorded in medical records. Furthermore, the limited number of years of data makes it difficult to use more accurate analysis methods to assess disease trends over time.

Acknowledgments:

The authors would like to thank the director and staff of Hadhramout National Oncology Center for their cooperation for making data available for our study.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-249.
2. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global Cancer Statistics, 2012. CA CANCER J CLIN. 2015; 65:87–108. Available at: https://doi.org/10.3322/caac.21262 PMID: 25651787
3. Ferlay J, Ervik M, Lam F, et al. eds, Global Cancer Observatory: Cancer Today (Version 1.0). International Agency for Research on Cancer; 2024. Available at: https://gco.iarc.who.int/ today.
4. Franco FL, Franco ED, Ferenczy A. Cervical cancer epidemiology, prevention and the role of human papillomavirus infection. CMAJ 2001; 164:1017-25.
5. World Health Organization. Cervical cancer. (cited 2024 March 4). Available from: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
6. Fowler JR, Maani EV, Jack BW. Cervical Cancer. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK431093/
7. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. Lyon, France: International Agency for Research on Cancer; 2013. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No.11.
8. Kent, A. HPV Vaccination and Testing. Obstetrics and Gynecology, 2010;3,33-34. Globocan (2008). International Agency For Research on Cancer, World Health Organization. Available at: http://globocan. iarc.fr/
9. Kemp Z, Ledermann JA. Update on first-line treatment of advanced ovarian carcinoma. International journal of women's health, 2013; 5:45-51,
10. Adeyemi AS, Afolabi AF, Adedeji OA. Ovarian cancer symptom awareness and its response among female health workers. Journal of Advances in Medicine and Medical Research,2015;5 (8):978-86.
11. Cancer research UK; UK ovarian cancer incidence statistics. Available at: http://info. cancer research.org. Cancer Status/types/ovary/incidence.
12. Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., Rebelo, M Parkin, D.M., Forman, D. and Bray, F. (2013) GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012 v1.0. IARC Press, Lyon, France
13. Liu L, Habeshian TS, Zhang J, Peeri NC, Du M, De Vivo I, Setiawan VW. Differential trends in rising endometrial cancer incidence by age, race, and ethnicity. JNCI Cancer Spectr. 2023; 03;7(1).
14. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, Nur U, Tracey E, Coory M, Hatcher J, et al: ICBP Module 1 Working Group: Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): An analysis of population-based cancer registry data. Lancet, 2011; 377: 127-138.
15. Gordhandas S, Zammarrelli WA, Rios-Doria EV, Green AK, Makker V. Current Evidence-Based Systemic Therapy for Advanced and Recurrent Endometrial Cancer. J Natl Compr Canc Netw. 2023;21(2):217-226.
16. Ellenson, L.H. and Pirog, E.C. The Female Genital Tract. In: Kumar, V., Abbas, A., Fausto, N. and Aster, J., Eds., Robbins and Cotran Pathologic Basis of Disease, Professional Edition, 8th Edition, Elsevier Saunders, Philadelphia, 2010;1005-1063. https://doi.org/10.1016/B978-1-4377-0792-2.50027-4
17. Sankaranarayanan R and Ferlay J: Worldwide burden of gynecological cancer: The size of the problem. Best Pract Res Clin Obstet Gynaecol 20: 207-225, 2006.
18. Osman Ortashi1 and Moza Al Kalbani. Gynecological Cancer Services in Arab Countries: Present Scenario, Problems and Suggested Solutions. Asian Pacific J Cancer Prev, 2013,14 (3),2147-2150.
19. Crane K. Cancer in the developing world: Palliative care gains ground in developing countries. J Natl Cancer Inst: 2010; 102(21):1613-5
20. Kulkarni A, Sun G, Manuppelli S, Mendez H, Rezendes J, Marin C, et al. Sexual health and function among patients receiving systemic therapy for primary gynecologic cancers. Gynecol Oncol. 2022; 165:323–9.
21. Gamal Abdul Hamid, Amani S. Hadi, Faten Al-Ahdel and Shada Yassin. Gynecological malignancies in Aden, Yemen: a four-year overview European Journal o f Pharmaceutical and Medical Research, 2018,5(10), 117-120.
22. Ibrahim Larbah, et al. Review of ovarian Cancer in Misurata Cancer Institute- Libya FIGO world congress, Cape Town –South Africa, 2009.
23. Nabila Javed, Rawail A. Khan, Mohammad Rauf Khattak, JavedIqbal, Pattern of gynecological malignancies at tertiary care hospital in Northwest region of Pakistan. International Journal of Development Research.2016;06,(01), 482-6485.

24. Haimanot E. Hailu, Alison M. Mondul, Laura S. Rozek, Temesgen Geleta. Descriptive Epidemiology of breast and gynecological cancers among patients attending Saint Paul's Hospital Millennium Medical College, Ethiopia. PLoS One 2020,20;15(3).
25. Bishal Khaniya .Histopathological Pattern of Gynecological Malignancies at Tribhuvan University Teaching Hospital, Nepal: A 3 Years Study. Nepalese Medical Journal, 2021; V. 4, 442-445.
26. Fabio Parazzini, Silvia Francesch, Carlo La Vecchi, Monica Fasol. The epidemiology of ovarian cancer Gynecologic Oncology, Volume 43, Issue 991, 9-23.
27. Li DP, Du C, Zhang ZM, Li GX, Yu ZF, Wang X, Li PF, Cheng C, Liu YP, Zhao YS. Breastfeeding and ovarian cancer risk: A systematic review and meta-analysis of 40 epidemiological studies. Asian Pac J Cancer Prev. 2014; 15(12):4829-37.
28. FramK. M. Albasha,A.S. Fram,F.K. Fram, R.K. Bishara, S. Abdillat, L.I. Approach of gynecological cancers at Jordan University Hospital: facts and figures.European Journal of Gynaecological Oncology. 2020;V.41,(1),89-92.
29. Humaid O Al-Shamsi , Faryal Iqbal, Mohd Subhi Al Saad, Priyanka Ashish Dhemre, Fady Georges Hachem, Mehdi Afrit, Ibrahim Abu-Gheida et al The Burden of Gynecologic Cancers in the UAE. Journal of Oncology Research Reviews & Reports 2021; V2(4): 1-6.
30. Liu Z, Zhang TT, Zhao JJ, Qi SF, Du P, Liu DW, Tian QB. The association between overweight, obesity and ovarian cancer: A meta-analysis. Japanese journal of clinical oncology. 2015; 45(12):1107-15.
31. Frederick W. Makoha and Muhamed A. Raheem. Gynecological cancer incidence in a hospital population in Saudi Arabia: The effect of foreign immigration over two decades. J. Obstet. Gynaecol. Res. 2008; V 34, (4): 538–542,
32. Sayma Afroz, Gulshan Ara, Fahmida Sultana. Pattern of Gynaecological Malignancies in a Tertiary Care Hospital. Journal of Obstetrics and Gynecology, 2019, 9, 449-457.
33. Chaudhary Sushila, Savita Rani Singhal, Latika, Anjali Gupta. Study of sociodemographic profile and pattern of gynaecological malignancies in a tertiary care center. International Journal of Reproduction, Contraception, Obstetrics and Gynecology 2016 ;5(8):2640-2643.
34. Osinachi I F., N. Adewole, A. D. Isah, H. I. Abdullahi and E. T. Agida. Pattern of gynaecological malignancies in a Nigerian tertiary hospital. African Journal of Medical and Health Sciences2020, V19 (3), 29-35.
35. Philip E Castle, Hossein H Ashrafi, Mustafa Ozdogan. Looking Back, Moving Forward: Challenges and Opportunities for Global Cervical Cancer Prevention and Control. National Center for Biotechnology information. 2024;16(9):1357. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC11435674/
36. Bibi S, Ashfaque S and Laghari NA: A heartrending burden of gynecological cancers in advance stage at nuclear institute of medicine and radiotherapy Jamshoro Sindh. Pak J Med Sci. 2016; 32: 120-124.
37. Agarwal S, Malhotra KP, Sinha S and Rajaram S: Profile of gynecologic malignancies reported at a tertiary care center in India over the past decade: Comparative evaluation with interna¬tional data. Indian J Cancer 2012; 49: 298-302,
38. Badar F, Mahmood S, Yusuf MA and Sultan F: Epidemiology of cancers in Lahore, Pakistan, 2010-2012: A cross-sectional study. BMJ, 2016; 21;7(12).
39. Nawal H. Almohammadi, The pattern of gynecological malignancies in Al-Madinah Al-Munawarah region, Saudi Arabia. An overview of 6 years. Saudi Med J 2022; Vol. 43 (3), 283-289.
40. Sahar Rostami, Azin Nahvijou1 Gynecologic Cancers Estimates in the I.R. Iran, 2012- 2040, Basic & Clinical Cancer Research 2021, 2, (13) :111-118.
41. Nasreen, F. Pattern of Gynaecological Malignancies in Tertiary Hospital. Journal of Postgraduate Medical Institute. 2002;16, 215-220.
42. Nnadi D, Sigh S, Ahmed Y, Siddique S, Bilal S. Histopathological features of genital tract malignancies as seen in a tertiary health center in north-western Nigeria: A 10 year review. Ann Med Health Sci Res, 2014; 4(3): 213-7.
43. Wasim T, Mushtaq J, Wasim AZ, Raana GE. Gynecological malignancies at tertiary care hospital, Pakistan: a five-year review. Pak J Med Sci 2021; 37: 621-627.
44. Khatun S, Ferdous J. Menopause and gynecological malignancy. JSAFOMS 2013; 1: 75-79.
45. Olaitan A., Mocroft A., Jacobs I.: "Patterns in the incidence of age related ovarian cancer in South East England 1967-1996". Br. J. Obstet. Gynaecol., 2000, 107, 1094.
46. Manzoor H, Naheed H, Ahmad K, Iftikhar S, Asif M, Shuja J, et al. Pattern of gynaecological malignancies in south western region of Pakistan: an overview of 12 years. Biomed Rep 2017; 7: 487-491.
47. Okunade , Kehinde S., Aloy O Ugwu, Adaiah Soibi-Harry, Sunusi G. Rimi, Olayemi Dawodu, Ephraim O. Ohazurike, et al. Pattern of Gynaecological Malignancies at a University Teaching Hospital in Southwest Nigeria: A 5-Year Review. Niger Med J,2022; 63(2):127 – 132.
48. Coburn S, Bray F, Sherman M, Trabert B. International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. Int J Cancer. 2017;140(11):2451–2460.
49. Stewart, B.W. and Kleihues, P. Cancers of female reproductive tract. In: World cancer report .IARC Press, Lyon, 2003; 232-236.
50. SEER Cancer Statistics Review. North American Association of Central Cancer Registries, Bethesda, Maryland, 1975-2007.Avialable at: https://seer.cancer.gov/data-software/
51. Boyle, P. and Ferlay, J. Cancer Incidence and Mortality in Europe, 2004.Annals of Oncology, 2005;16, 481-488. Available at https://doi.org/10.1093/annonc/mdi098.
52. Mehmat N.F., Talip G., Ahmed E.A.: "Distribution of gynecologic malignancies in an epidemiology study from southeast of Turkey. Eastern Journal of Medicine,2011; 16, 39.

53. Tanko MN, Kayembe MA, Cainelli F, Vento S. Malignant tumors of the genital tract among Batswana women. Ghana Med J 2012; 46: 142-146.
54. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023 Jan;73(1):17-48.
55. Brooks RA, Fleming GF, Lastra RR, Lee NK, Moroney JW, Son CH, Tatebe K, Veneris JL. Current recommendations and recent progress in endometrial cancer. CA Cancer J Clin. 2019 Jul;69(4):258-279.
56. Tham BW, Everrard JE, Tidy JA, Drew D and Hancock BW: Gestational trophoblastic disease in the Asian population of Northern England and North Wales. An International Journal of Obstetrics & Gynecology, 2003;110:555-559.
57. Gultekin M, Kucukyildiz I, Karaca MZ, Dundar S, Boztas G, Turan SH, et al. Trends of gynecological cancers in Turkey: Toward Europe or Asia? Int J Gynecol Cancer 2017; 27: 1525-1533.
58. Ojamaa K. Epidemiology of gynecological cancer in Estonia. University of Tartu 2019.
59. Nkyekyer K. Pattern of gynecological cancers in Ghana. East African Medical Journal; 2000: 534-538.
60. Althubiti MA, Nour Eldein MM. Trends in the incidence and mortality of cancer in Saudi Arabia. Saudi Med J. 2018 ;39(12):1259-62.
61. Rufei Duan, Hongping Zhang, Jing Yu, Sisi Deng, Haijun Yang, Yong-Tang Zheng, Yunchao Huang et al. Temporal trends and projections of gynecological cancers in China, 2007–2030.BMC Women's Health, 2023; v 23: 346.
62. Iyoke CA, Ugwu GO. Burden of gynecological cancers in developing countries. World J Obstet Gynecol 2013; 2(1): 1-7.