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Confronting Health Challenges Across Disciplines — From Chronic Disease to Social Determinants

The manuscripts in this collection traverse a wide range of pressing health issues, yet they share a unifying theme: the interplay of medical science, clinical practice, and societal factors in shaping human well-being. From chronic disease management and rare diagnostic challenges to social determinants of health and maternal awareness, the papers collectively demonstrate that effective healthcare requires a holistic approach that integrates biological, psychological, and cultural dimensions.

Obesity and hypertension, among the most prevalent risk factors for global morbidity, remain at the forefront. Beyond their metabolic consequences, obesity carries the added burden of stigma, with patients often facing discrimination in healthcare and society at large, leading to poorer outcomes and delays in care. Similarly, gaps in hypertension management persist, as seen in audits showing underuse of guideline-recommended assessments; however, structured electronic tools demonstrate that small systemic changes can significantly improve compliance and patient outcomes. Together, these works remind us that treating chronic disease requires not only effective therapeutics but also attention to the environments—clinical and social—in which patients live.

Clinical vigilance is emphasized in case-based insights, such as the report of celiac disease presenting solely as liver enzyme elevation, underscoring the need to consider seronegative presentations when standard serology is negative. At the other end of the spectrum, innovation in therapeutics raises both hope and caution. Tirzepatide, hailed as a breakthrough in weight and diabetes management, demonstrates unparalleled efficacy in weight loss and glycemic control, yet long-term cancer and pancreatitis risks remain inadequately understood. Similarly, reflections on older agents such as acarbose in preventing stroke place established therapies in new preventive contexts, highlighting the evolving nature of clinical application.

The burden of aging is powerfully represented through dementia and bone health. A comprehensive overview of dementia reminds us that cognitive decline is not inevitable with aging, and that subtypes such as Alzheimer's disease, vascular dementia, and Lewy body dementia pose unique diagnostic and management challenges. The rising prevalence has profound implications for patients, families, and healthcare systems worldwide. Complementary to this, research into vitamin D deficiency and fracture patterns in Saudi Arabia underscores how lifestyle, cultural practices, and limited sun exposure contribute to fragility fractures, especially among younger populations and women. Together, these findings illuminate the urgent

need for preventive strategies in aging societies.

Maternal and child health emerges as another crucial theme. The study of primary healthcare physicians in Saudi Arabia revealed strong theoretical knowledge of gestational diabetes but limited practical engagement, underscoring the gap between training and real-world implementation. The paper on maternal awareness of child trauma adds another dimension, showing that despite the high burden of injuries—falls, burns, and accidents—maternal awareness of first aid and prevention remains inadequate. This gap underscores the need for education programs to empower families, as child trauma not only carries immediate risks but also long-term consequences for development, chronic disease vulnerability, and mental health.

Health is also shaped by culture, economics, and media. The reflection on cosmetic surgery highlights the dangers of unregulated interventions such as the Brazilian Butt Lift, fueled by social media and unrealistic body ideals. Equally, food insecurity and consumer responses to rising egg prices in the U.S. illustrate how economic shocks reshape dietary patterns, disproportionately affecting low-income and minority communities and raising broader questions of equity and resilience in food systems.

Taken together, these diverse contributions reveal medicine not as a series of isolated disciplines but as a deeply interconnected ecosystem. Chronic disease management cannot be divorced from stigma and culture; maternal and child health requires both clinical expertise and community education; therapeutics must balance innovation with vigilance for long-term safety; and societal trends—from social media to food inflation—bear directly on health outcomes.

The collective message of this issue is clear: progress in health demands an integrated approach that bridges biomedical research, clinical vigilance, social awareness, and policy innovation. By weaving these strands together, we can move toward a more responsive, equitable, and effective healthcare landscape—one that honors the complexity of human health while striving for tangible improvements in quality of life.

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

Knowledge, Attitudes, and Practices of Primary Health Care Physicians toward Gestational Diabetes Mellitus in Tabuk City, Saudi Arabia

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Abstract

Background: Gestational Diabetes Mellitus (GDM) is a common pregnancy-related condition associated with adverse maternal and neonatal outcomes. Primary health care (PHC) physicians play a critical role in early detection and management of GDM.

Aim: This study aimed to assess the knowledge, attitudes, and practices (KAP) of PHC physicians regarding GDM in Tabuk City, Saudi Arabia.

Methods: A cross-sectional study was conducted among 102 PHC physicians working under the Ministry of Health in Tabuk between May and December 2024. Data were collected using a structured, self-administered questionnaire covering socio-demographics, knowledge, attitudes, and practices related to GDM. Descriptive statistics and the Exact Probability Test were used for data analysis using SPSS version 28. A 60% cutoff was used to categorize knowledge as poor or good.

Results: The majority of physicians were aged 30–40 years and had over five years of experience. Most (98%) demonstrated acceptable knowledge of GDM, with 91.2% achieving a good overall knowledge score. Female physicians and those with higher qualifications were more likely to have good knowledge. While 95.1% believed PHC physicians have an active role in GDM management, 74.5% found it difficult to diagnose or manage. In practice, only 34.3% had diagnosed GDM cases in the past year, and most referred patients to specialists. Significant associations were found between knowledge and both qualification ($p = 0.041$) and CME attendance ($p = 0.049$).

Conclusion: PHC physicians in Tabuk have a strong theoretical understanding of GDM and show positive attitudes toward its management, though practical involvement remains limited. Strengthening training programs, clarifying clinical roles, and enhancing referral systems are recommended to support effective GDM management at the primary care level.

Keywords
Gestational Diabetes Mellitus (GDM); Primary Health Care; Physicians; Knowledge; Attitudes; Practices; Tabuk; Saudi Arabia; Screening; Maternal Health; CME; Referral.

Introduction

Diabetes is a long-term metabolic disorder featured by elevated blood glucose levels, which, over time, can lead to serious complications affecting the cardiovascular system, kidneys, eyes, nerves, and blood vessels [1, 2]. In 2019, the global prevalence of diabetes was estimated at 9.3%, with projections indicating a rise to 10.9% by the year 2030 [3]. Gestational diabetes mellitus [GDM] is a specific form of glucose intolerance that is first recognized during pregnancy [4]. It is considered the most common complication of pregnancy and poses significant risks to both maternal and fetal health. For the mother, GDM increases the risk of conditions such as preeclampsia and the future development of type 2 diabetes [5]. For the infant, maternal hyperglycemia is associated with increased risks of congenital anomalies, delivery complications, and Macrosomia [excessive birth weight] [6].

In Saudi Arabia, a study by Al-Rifai et al. in 2021 estimated the prevalence of GDM to be 15.5% [7]. Risk factors that increase the likelihood of developing GDM include a family history of diabetes, obesity, previous history of GDM, and rapid weight gain during pregnancy [8].

Screening guidelines recommend early testing before 24 weeks of gestation for women at high risk, while routine screening for low-risk, asymptomatic women is advised after 24 weeks [9]. In the United States, the American College of Obstetricians and Gynecologists [ACOG] recommends a two-step approach involving a 50g oral glucose challenge test [OGCT], followed if necessary by a 100g, 3-hour oral glucose tolerance test [OGTT] [10]. A diagnosis of GDM is made when two or more values exceed the diagnostic thresholds. Conversely, many other countries follow a one-step approach, using a fasting 75g, 2-hour OGTT without prior screening [11]. A single abnormal result in this test is sufficient for diagnosis [10, 11].

First-line management of GDM typically includes lifestyle interventions such as dietary changes and regular physical activity [12]. If these measures are insufficient to control blood glucose, insulin therapy may be introduced [13]. However, effective management also requires counseling and patient education to reduce risks and improve outcomes [14]. Women diagnosed with GDM face multiple risks, including neonatal hypoglycemia, Macrosomia, and a higher likelihood of primary cesarean delivery [15]. This study aimed to assess the knowledge, attitudes, and practices [KAP] of primary health care physicians regarding gestational diabetes mellitus in Tabuk City, Saudi Arabia.

Methodology

A cross-sectional study design was conducted in Primary Health Care Centers [PHCCs] in Tabuk City, Saudi Arabia. These centers provide various services including health promotion, health education, immunization, and routine screenings to all age groups. The centers comprise specialized clinics such as the Well-Baby Clinic, Chronic Disease Clinic, Maternal Health Clinic, Health Education Clinic, and Emergency Clinic. The study targeted primary health care physicians, including both family medicine physicians and general practitioners, working in PHCCs under the Ministry of Health in Tabuk City. Physicians working outside PHCCs or not affiliated with the Ministry of Health, as well as specialists other than family medicine or general practitioners, were excluded. Data collection took place between May 2024 and December 2024. Based on the total population of 414 PHC physicians in Tabuk, and using a 95% confidence interval with a 5% margin of error, the required sample size was calculated to be 200 physicians using the Raosoft sample size calculator. A convenience sampling technique was used to recruit participants. Data were gathered using a self-administered questionnaire that was developed based on previously published studies on GDM. The questionnaire consisted of four main sections: [1] demographic information [e.g., age, gender, nationality, job title, and years of experience, CME attendance, and GDM case exposure]; [2] items assessing knowledge about GDM; [3] questions regarding attitudes toward GDM; and [4] items evaluating clinical practice related to GDM. The questionnaire was reviewed by four family medicine consultants to ensure clarity and relevance, though it was not formally validated.

A pilot study was conducted on a purposive sample of 25 primary health care physicians from Tabuk's Ministry of Health facilities. Data from this pilot were excluded from the main analysis. The pilot aimed to assess the clarity and reliability of the questionnaire, resulting in necessary adjustments before final implementation.

Data Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 28.0 [IBM Corp., Armonk, NY, USA]. Descriptive statistics were used to summarize the socio-demographic characteristics, knowledge, attitudes, and practices of primary health care physicians regarding Gestational Diabetes Mellitus [GDM]. Categorical variables were presented as frequencies and percentages. The overall knowledge score was calculated based on responses to the knowledge items where each correct answer was scored 1 point. A cutoff point of 60% was used to categorize participants into two groups: poor knowledge [<60%] and good knowledge [≥60%].

Associations between physicians' knowledge levels and their demographic characteristics, attitudes, and practices were examined using the Exact Probability Test [Fisher's Exact Test] due to the small cell sizes in some categories. A p-value less than 0.05 was considered statistically significant.

Results

Table 1: Socio-Demographic Characteristics of the Study Primary Health Care Physicians, Tabuk, Saudi Arabia (N=102)

Table 1 presents the socio-demographic characteristics of 102 primary health care physicians in Tabuk, Saudi Arabia. The majority of participants [53 physicians; 52.0%] were aged between 30 and 40 years, while 38 physicians [37.3%] were under 30 years, and a smaller proportion [11 physicians; 10.8%] were over 40 years. Female physicians slightly outnumbered males, with 55 [53.9%] females compared to 47 [46.1%] males. Regarding nationality, most participants were Saudi [64; 62.7%], while 38 [37.3%] were non-Saudi. Regarding academic qualifications, 62 physicians [60.8%] held an MBBS degree, while 20 physicians each [19.6% for both] had either a Diploma/Master's or Doctorate degree. As for professional experience, the majority [73; 71.6%] had five or more years of experience in health care, while 29 [28.4%] had less than five years. Importantly, almost all participants demonstrated an acceptable level of knowledge regarding GDM, with 100 physicians [98.0%] showing acceptable knowledge and only 2 [2.0%] showing poor knowledge.

Demographics	No	%
Age in years		
<30	38	37.3%
>40	11	10.8%
30-40	53	52.0%
Gender		
Male	47	46.1%
Female	55	53.9%
Nationality		
Saudi	64	62.7%
Non Saudi	38	37.3%
Qualification		
MBBS	62	60.8%
Diploma / Master	20	19.6%
Doctorate	20	19.6%
Experience in health care		
< 5 years	29	28.4%
>= 5 years	73	71.6%
Participants' knowledge level of GDM		
Poor	2	2.0%
Acceptable	100	98.0%

Table 2 highlights the knowledge and awareness of 102 primary health care physicians in Tabuk, Saudi Arabia, regarding Gestational Diabetes Mellitus [GDM]. The majority of respondents [98; 96.1%] correctly defined GDM as “glucose intolerance with onset or first recognition during pregnancy,” A high proportion of physicians [97; 95.1%] reported awareness of GDM symptoms. Among those, 37 [38.1%] identified asymptomatic presentation, 35 [36.1%] mentioned hyperglycemia, 19 [19.6%] noted polyuria, and 6 [6.2%] selected other symptoms. Regarding risk factors, 94 physicians [92.2%] responded positively. Among those, personal history of GDM was the most recognized risk factor [75; 79.8%], followed by family history [32; 34.0%], obesity [10; 10.6%], and others [3; 3.2%]. Regarding maternal complications, cesarean delivery was the most frequently recognized [95; 93.1%], followed by pre-eclampsia [82; 80.4%], pregnancy-induced hypertension [45; 44.1%], and postpartum depression [40; 39.2%]. For neonatal complications, physicians commonly selected Macrosomia [97; 95.1%], shoulder dystocia [88; 86.3%], respiratory distress syndrome [71; 69.6%], and to a lesser extent, hypoglycemia [9; 8.8%]. Most physicians correctly identified the screening window for GDM as 24–28 weeks [97; 95.1%], and the appropriate screening test as the 75g OGTT [99; 97.1%]. The majority [86; 84.3%] correctly identified venous blood sampling as the method used, while others selected plasma [11; 10.8%] or capillary samples [5; 4.9%]. Awareness of diagnostic criteria was high [91; 89.2%]. Regarding initial management, 73 [71.6%] correctly selected “all of the above” [dietary modifications and physical activity], while 18 [17.6%] chose physical activity only and 9 [8.8%] chose dietary modifications alone. As for treatment, insulin was the most commonly known medication [82; 80.4%], followed by metformin [19; 18.6%] and glyburide [1; 1.0%]. Nearly all participants [101; 99.0%] agreed that it is mandatory to educate pregnant women about GDM.

Table 2: Knowledge and Awareness of Primary Health Care Physicians Regarding Gestational Diabetes Mellitus (GDM) in Tabuk, Saudi Arabia (N = 102)

Knowledge items		No	%
Which of the following is a definition of GDM?	Glucose intolerance with onset or first recognition during pregnancy	98	96.1%
	Pressure condition in which a woman has high blood pressure during pregnancy	2	2.0%
	Chronic diabetes in pregnant woman	2	2.0%
Do you know about symptoms of GDM?	Yes	97	95.1%
	No	5	4.9%
If yes, report symptoms?	Polyuria	19	19.6%
	Hyperglycemia	35	36.1%
	Asymptomatic	37	38.1%
	Others	6	6.2%
Do you know about risk factors for developing GDM?	Yes	94	92.2%
	No	8	7.8%
What are the risk factors	Personal history of GDM	75	79.8%
	Family history of GDM	32	34.0%
	Obesity	10	10.6%
	Others	3	3.2%
Which of the following are possible complications of GDM for the mother?	Cesarean delivery	95	93.1%
	Pre-eclampsia	82	80.4%
	Pregnancy-induced hypertension	45	44.1%
	Postpartum depression	40	39.2%
Which of the following are possible complications of GDM for the baby?	Macrosomia	97	95.1%
	Hypoglycemia	9	8.8%
	Respiratory distress syndrome	71	69.6%
	Shoulder dystocia	88	86.3%
What is the best time to screen for GDM for pregnant woman?	24-28 weeks of gestational age	97	95.1%
	1st visit during 1st trimester	4	3.9%
	3rd trimester	1	1.0%
What is the test used for screening for GDM?	75 OGTT	99	97.1%
	Fasting blood glucose	1	1.0%
	RBS	1	1.0%
	HbA1c	1	1.0%
How to take blood sample?	Venous blood sample	86	84.3%
	Plasma blood sample	11	10.8%
	Capillary blood sample	5	4.9%
Do you know about diagnostic criteria of GDM?	Yes	91	89.2%
	No	11	10.8%
Which of the following initial management strategies do you know about GDM?	Physical activity	18	17.6%
	Dietary modifications	9	8.8%
	All of the above	73	71.6%
	None of the above	2	2.0%
What is the type of medical treatment for GDM?	Insulin	82	80.4%
	Metformin	19	18.6%
	Glyburide	1	1.0%
Do you think it is mandatory to educate pregnant women about GDM?	Yes	101	99.0%
	No	1	1.0%

Figure 1 presents the overall knowledge and awareness levels of 102 primary health care physicians in Tabuk, Saudi Arabia, regarding Gestational Diabetes Mellitus [GDM], along with their sources of information. The majority of physicians [93; 91.2%] had a good overall knowledge level, while only a small fraction [9; 8.8%] had poor knowledge. Regarding sources of knowledge [Figure 2], the most commonly reported source was self-reading [96; 94.1%], followed by the internet [46; 45.1%] and continuing medical education [CME] activities [27; 26.5%].

Figure 1: The Overall Knowledge and Awareness of Primary Health Care Physicians Regarding Gestational Diabetes Mellitus (GDM) in Tabuk, Saudi Arabia (N = 102)

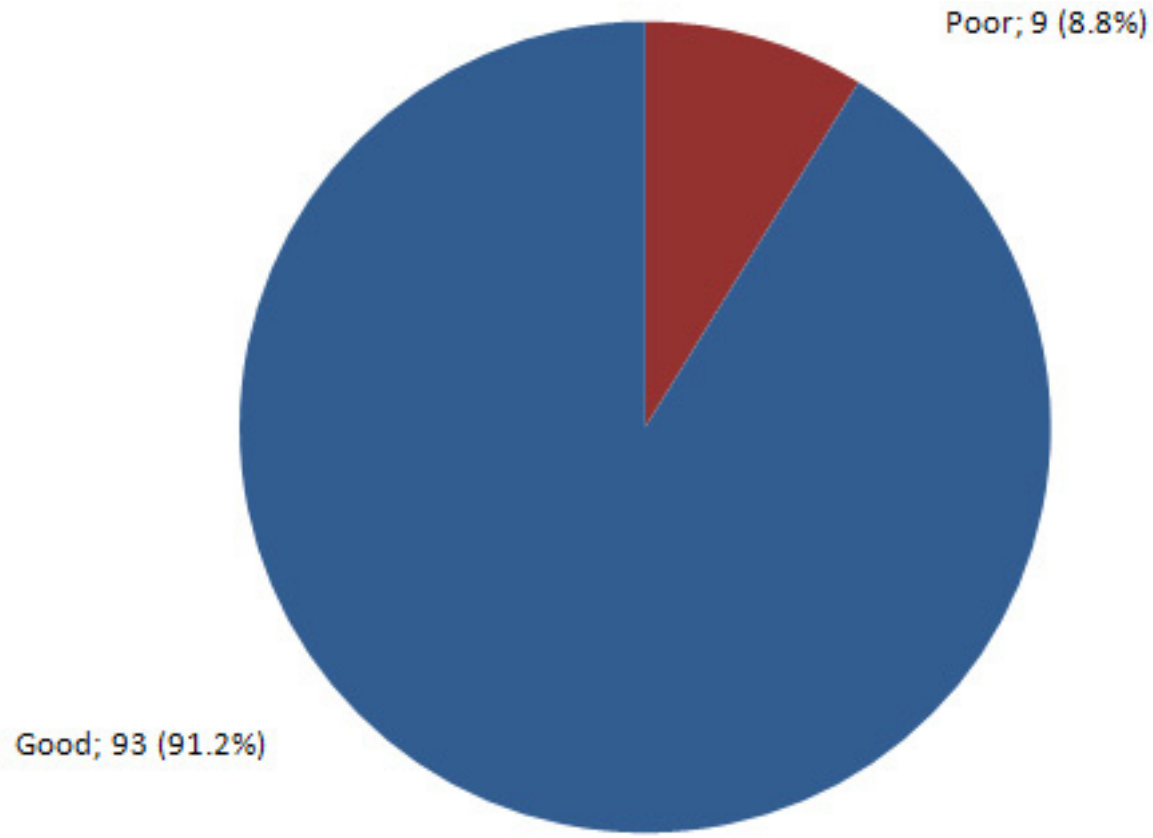

Figure 2. The Source of Knowledge about GDM among the Study Physicians

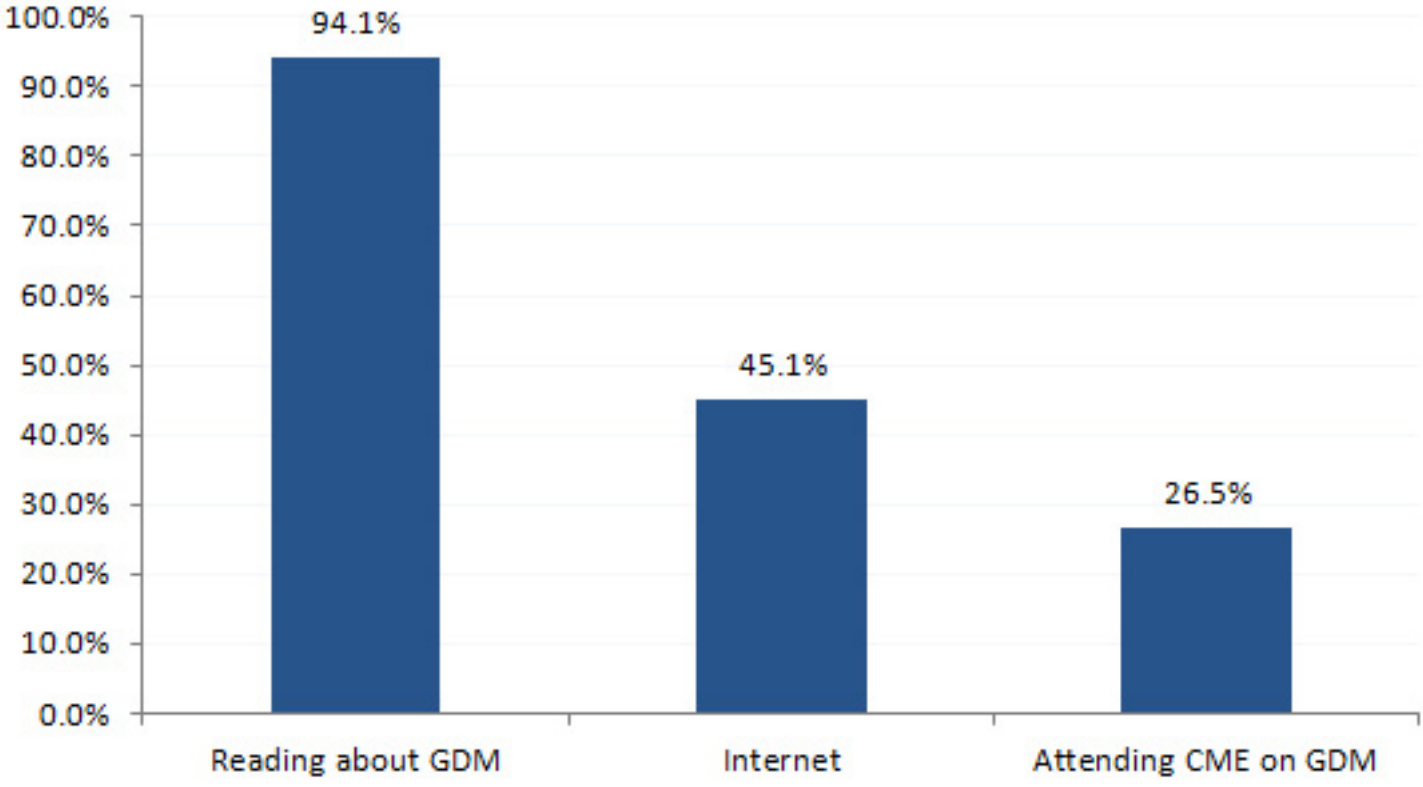

Table 3 presents the attitudes of 102 primary health care [PHC] physicians in Tabuk toward the diagnosis and management of Gestational Diabetes Mellitus [GDM]. A considerable number of respondents [76; 74.5%] agreed that GDM is difficult to diagnose or manage at the PHC level. Despite this, a large majority [97; 95.1%] believed that PHC physicians can play an active role in GDM management. Interestingly, 80 physicians [78.4%] disagreed with the statement that "management of GDM is not the job for PHC physicians," reinforcing the belief that GDM falls within their scope of practice. Additionally, 87 participants [85.3%] agreed that suspected cases of GDM should be referred to a diabetic center.

Table 3. Attitudes of Primary Health Care Physicians toward the Diagnosis and Management of Gestational Diabetes Mellitus (GDM) in Tabuk, Saudi Arabia (N = 102)

Attitude	Agree		Disagree	
	No	%	No	%
GDM is difficult to diagnose or manage by PHC physicians	76	74.5%	26	25.5%
PHC physicians can play an active role in the management of GDM	97	95.1%	5	4.9%
Management of GDM is not the job for PHC physicians	80	78.4%	22	21.6%
For the diagnosis of GDM in pregnant women, PHC physicians should refer any suspected case to diabetic center	87	85.3%	15	14.7%

Table 4 shows the practical experience of 102 primary health care [PHC] physicians in Tabuk concerning the diagnosis and management of Gestational Diabetes Mellitus [GDM]. Only 35 physicians [34.3%] reported diagnosing GDM cases within the past year, while the majority [67; 65.7%] had not encountered such cases, which may indicate either a low case detection rate at the PHC level or reliance on specialist centers for diagnosis. Among those who diagnosed GDM, most physicians [29; 82.9%] referred patients to specialists, while only a small proportion [6; 17.1%] reported prescribing treatment themselves.

Table 4: Practice of Primary Health Care Physicians Regarding Diagnosis and Management of Gestational Diabetes Mellitus (GDM) in Tabuk, Saudi Arabia (N = 102)

Practice	No	%
Did you diagnose case(s) with GDM in the last year		
Yes	35	34.3%
No	67	65.7%
Action after diagnosing the cases		
Prescribed treatment to GDM patients	6	17.1%
Refer GDM patients to a specialist	29	82.9%

Table 5 explores the association between various factors and the overall knowledge level of primary health care physicians regarding Gestational Diabetes Mellitus [GDM] in Tabuk. Among the demographic factors, gender showed a statistically significant association with knowledge level [p = 0.046]. Female physicians had a higher rate of good knowledge [96.4%] compared to males [85.1%]. Qualification also demonstrated a significant association [p = 0.041], where all physicians with a Diploma/Master or Doctorate showed 100% good knowledge, compared to 85.5% among those with only an MBBS degree. Sources of knowledge were another significant factor [p = 0.049]. Physicians who attended CME on GDM had the highest proportion of good knowledge [96.3%], followed closely by those who relied on the internet [93.5%] and self-reading [92.7%]. In contrast, other factors such as age [p = 0.603], nationality [p = 0.329], years of experience [p = 0.265], and whether the physician diagnosed GDM in the past year [p = 0.424] did not show statistically significant associations with knowledge level.

Table 5: Factors Associated with Primary Health Care Physicians Knowledge about GDM in Tabuk (N=102)

Factors	Overall knowledge level				p-value
	Poor		Good		
	No	%	No	%	
Age in years					
<30	2	5.3%	36	94.7%	.603
>40	1	9.1%	10	90.9%	
30-40	6	11.3%	47	88.7%	
Gender					
Male	7	14.9%	40	85.1%	.046*
Female	2	3.6%	53	96.4%	
Nationality					
Saudi	7	10.9%	57	89.1%	.329
Non Saudi	2	5.3%	36	94.7%	
Qualification					
MBBS	9	14.5%	53	85.5%	.041*
Diploma / Master	0	0.0%	20	100.0%	
Doctorate	0	0.0%	20	100.0%	
Experience in health care					
< 5 years	4	13.8%	25	86.2%	.265
>= 5 years	5	6.8%	68	93.2%	
Sources of knowledge regarding GDM					
Reading about GDM	7	7.3%	89	92.7%	.049*
Internet	3	6.5%	43	93.5%	
Attending CME on GDM	1	3.7%	26	96.3%	
Did you diagnose case(s) with GDM in the last year					.424
Yes	2	5.7%	33	94.3%	
No	7	10.4%	60	89.6%	

P: Exact Probability test * P < 0.05 (significant)

Table 6 presents the association between the attitudes of primary health care [PHC] physicians and their overall knowledge level regarding Gestational Diabetes Mellitus [GDM] in Tabuk. A statistically significant association was observed between the belief that PHC physicians can play an active role in the management of GDM and a higher knowledge level [p = 0.012]. Among physicians with good knowledge, 96.8% agreed with this statement compared to 77.8% of those with poor knowledge. Similarly, a significant association was found regarding the attitude that "management of GDM is not the job for PHC physicians" [p = 0.009]. Interestingly, a higher percentage of physicians with good knowledge [81.7%] agreed with this statement compared to 44.4% among those with poor knowledge. Other attitudes, such as believing that GDM is difficult to diagnose/manage [p = 0.172] and that suspected GDM cases should be referred to a diabetic center [p = 0.098], did not show statistically significant associations with knowledge level.

Table 6: Association between Primary Health Care Physicians' Attitudes and their Knowledge Level about Gestational Diabetes Mellitus (GDM) in Tabuk, Saudi Arabia (N = 102)

Attitude	Overall knowledge level				p-value
	Poor		Good		
	No	%	No	%	
GDM is difficult to diagnose or manage by PHC physicians					.172
Agree	5	55.6%	71	76.3%	
Disagree	4	44.4%	22	23.7%	
PHC physicians can play an active role in the management of GDM					.012*
Agree	7	77.8%	90	96.8%	
Disagree	2	22.2%	3	3.2%	
Management of GDM is not the job for PHC physicians					.009*
Agree	4	44.4%	76	81.7%	
Disagree	5	55.6%	17	18.3%	
For the diagnosis of GDM in pregnant women, PHC physicians should refer any suspected case to diabetic center					.098
Agree	6	66.7%	81	87.1%	
Disagree	3	33.3%	12	12.9%	

P: Exact Probability test
* P < 0.05 (significant)

Discussion

The study found that most primary health care physicians in Tabuk were young to mid-career professionals, mainly aged 30–40 years, with a slight female majority. While most were Saudi nationals, a significant portion were non-Saudi, reflecting workforce diversity. The majority held MBBS degrees, with fewer holding advanced qualifications. Most had over five years of experience, which likely supports clinical competence. Encouragingly, almost all physicians showed acceptable knowledge of GDM, indicating a strong theoretical foundation.

Regarding knowledge level, the findings of this study revealed that primary health care physicians in Tabuk, Saudi Arabia, showed a high level of knowledge regarding gestational diabetes mellitus (GDM), with nearly all participants indicating acceptable knowledge. This contrasts with studies from other regions, where knowledge gaps and inconsistent adherence to guidelines were more prevalent. For instance, in a 2017 Moroccan study, only 70% of healthcare providers had a basic understanding of GDM, and adherence to screening guidelines was as low as 50% [16]. Similarly, a 2018 study in rural India found that only 30% of physicians routinely screened for GDM, and 40% were unaware of updated management guidelines [17]. The high knowledge levels among Tabuk physicians may be attributed to structured medical education and continuous professional development initiatives in Saudi Arabia, which appear more effective than in some other settings.

The demographic profile of participants in this study primarily mid-career physicians [aged 30–40] with substantial clinical experience [71.6% having ≥5 years of practice] may also contribute to their strong foundational knowledge. This matches with findings from Ohio, USA, where more experienced physicians were more likely to follow GDM screening guidelines, though adherence remained inconsistent [only 60% screened high-risk women appropriately] [18]. The fact that most Tabuk physicians held an MBBS degree [60.8%] rather than advanced qualifications suggests that undergraduate and in-service training in Saudi Arabia may sufficiently cover GDM, unlike in other regions where additional training has been recommended [16, 17].

However, while knowledge levels were high, this study did not assess actual clinical practices, leaving a gap in understanding whether theoretical knowledge translates into effective GDM management. Previous research highlights that even when knowledge is adequate, implementation can lag. For example, in Morocco, despite moderate knowledge levels, only 40% of providers followed consistent management practices [16]. Similarly, in Ohio, despite reasonable awareness, 25% of physicians were unfamiliar with postpartum screening guidelines [18]. This suggests that future research in Saudi Arabia should evaluate practice patterns to determine if knowledge correlates with guideline adherence.

Comparisons with patient-focused studies, such as those in China [19] and Jeddah [20], reveal that while healthcare providers may have strong knowledge, patient awareness varies significantly based on education level. In Jeddah, only 60% of highly educated pregnant women had good GDM comprehension, compared to 30% among less-educated women [20]. This highlights the need for targeted patient education alongside provider training to ensure comprehensive GDM care.

The study also revealed key factors influencing GDM knowledge among primary care physicians in Tabuk. Gender was significantly associated with knowledge, with female physicians demonstrating higher competency compared to males. This aligns with some studies suggesting that female providers may prioritize maternal health education more actively [13, 21]. Academic qualification also played a critical role as physicians with advanced degrees (Diploma/Master's/Doctorate) universally showed excellent knowledge, whereas MBBS holders had slightly lower rates. This underlines the impact of postgraduate training in enhancing GDM expertise, consistent with findings from Morocco where specialized training improved guideline adherence [16].

Sources of knowledge further differentiated performance: those attending CME sessions or using internet/self-reading outperformed peers relying on other sources. This highlights the effectiveness of structured education and self-driven learning, mirroring recommendations from India and the U.S. for continuous professional development [17, 22]. Age, nationality, experience, and prior GDM diagnosis showed no significant links to knowledge, contrasting with some studies where experience correlated with better practices.

The study assessed the primary care physicians' attitudes toward GDM management in Tabuk. Although most of them viewed GDM as difficult to diagnose and manage at the primary care level, the vast majority still believed they had an active role to play. This reflects a strong sense of professional responsibility despite perceived challenges. Most physicians disagreed with the idea that GDM management is not part of their role, showing strong commitment to involvement in care. While many referred suspected cases to diabetic centers, this indicates an appropriate balance between primary care responsibility and the need for specialist support. These attitudes are consistent with Saudi Arabia's healthcare structure, where primary care acts as the first point of contact. The findings reflect that with improved training, clearer protocols, and strengthened referral systems, PHC physicians could be even more effective in managing GDM. Notably, their positive attitudes contrast with other settings where primary care providers often feel less prepared to manage GDM, likely reflecting Saudi Arabia's focus on strengthening its primary healthcare system.

Conclusion and Recommendations

This study revealed that primary health care physicians in Tabuk generally demonstrated a high level of knowledge and awareness regarding gestational diabetes mellitus (GDM). Most physicians correctly identified key aspects of GDM, including risk factors, complications, screening windows, and management strategies. Their knowledge was significantly associated with gender, qualification level, and participation in continuing medical education. Although attitudes were largely positive, a substantial number perceived GDM as difficult to manage at the PHC level, and most preferred to refer diagnosed cases to specialists, indicating some limitations in practical involvement. It is recommended to enhance GDM-related training programs and clinical guidelines tailored for PHC settings. Clear referral protocols and strengthened collaboration between primary and specialized care are essential to ensure continuity and quality of care. These strategies can support PHC physicians in translating their knowledge and attitudes into effective clinical practice, ultimately improving maternal and neonatal outcomes.

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Acarbose in prevention of stroke

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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 lives (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), stroke (12.1% vs 7.5%, p<0.05), chronic renal disease (CRD) (9.9% vs 6.1%, p<0.05), cirrhosis (8.1% vs 1.8%, p<0.001), chronic obstructive pulmonary disease (25.2% vs 7.0%, p<0.001), coronary heart disease (18.0% vs 13.2%, p<0.05), leg ulcers (19.8% vs 7.0%, p<0.001), and clubbing (14.8% vs 6.6%, p<0.001) were all higher in males.

Conclusion: As an accelerated atherosclerotic process, hardened RBC-induced capillary endothelial damage initiated at birth terminates with multiorgan failures in early decades in SCD. Excess fat may be more important than smoking and alcohol for atherosclerosis since excess weight-induced diabetes mellitus is the most common cause of the CRD. The efficacy of acarbose to lower blood glucose by preventing breakdown of starch into sugar in the small intestine is well-known. Since acarbose is a safe, cheap, oral, long-term used, and effective drug for excess weight, it should be prescribed in prevention of stroke, particularly after the age of 50 years even in cases with normal weight because there are nearly 19 kg of excess fat even between the lower and upper borders of normal weight in adults.

Key words: Sickle cell diseases, stroke, acarbose, capillary endothelial inflammation, excess fat tissue, systemic atherosclerosis, smoking

Introduction

Chronic endothelial damage, initiated at birth, may be the main cause of aging and death via the atherosclerotic multiorgan deficiencies in human being (1). Much higher blood pressures (BP) of the afferent vasculature may be the strongest accelerating factor by means of repeated damages on vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the destructive process. Therefore venosclerosis is not a significant health problem. Because of the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose elastic natures, which eventually reduce blood supply to the terminal organs, and increase systolic and decrease diastolic BP further. Some of the clear accelerating factors of the inflammatory process are physical and mental inactivity, animal-rich diet, emotional stresses, smoking, alcohol, excess fat tissue, chronic inflammation, prolonged infection, and cancers for the development of terminal endpoints including obesity, hypertension (HT), diabetes mellitus (DM), chronic renal disease (CRD), coronary heart disease (CHD), cirrhosis, chronic obstructive pulmonary disease (COPD), peripheric artery disease (PAD), stroke, mesenteric ischemia, osteoporosis, dementia, early aging, and premature death (2, 3). Although early withdrawal of the accelerating factors can delay the endpoints, the endothelial changes can not be reversed, completely due to fibrotic natures of the endpoints after development of them. The accelerating factors and terminal endpoints of the destructive process on vascular endothelium are researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome (4-6). Similarly, sickle cell diseases (SCD) are highly destructive process on vascular endothelial cells, initiated at birth and terminated with an accelerated atherosclerosis-induced multiorgan failures in much earlier decades of life (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 survival is not affected in hereditary spherocytosis or elliptocytosis in human being. Loss of elasticity is present in whole lifespan, but exaggerated with inflammation, infection, cancer, or additional stresses. The hardened RBC-induced chronic endothelial damage, inflammation, edema, and fibrosis terminate with tissue hypoxia all over the 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 main distributor of the hardened RBC (10, 11). The hardened RBC-induced chronic endothelial damage builds up an accelerated atherosclerosis in earlier decades of life. Vascular narrowing and occlusions-induced tissue ischemia and multiorgan failures are the final endpoints, so the mean life expectancy is decreased 30 years or more in Turkey in the SCD since we have patients with the age of 96 years without the SCD but just 59 years with the SCD (8).

Material and Methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and June 2016. All patients with the SCD were included into the study. SCD are diagnosed with the hemoglobin electrophoresis performed via high performance liquid chromatography (HPLC). 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 in the patients. Patients with a history of one pack-year and one drink-year were accepted as smoker and drinkers, respectively. A full physical examination was performed by the Same Internist, and cases with disseminated teeth losses (<20 teeth present) were detected. Patients with acute painful crisis or any other inflammatory or infectious process 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 via HPLC since 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, laboratory parameters, and ultrasonographic evaluation of the liver. The criterion for diagnosis of COPD is a post-bronchodilator forced expiratory volume in one second/forced vital capacity of lower than 70% (15). Acute chest syndrome (ACS) is diagnosed clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum, dyspnea, 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 is diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity. CRD is diagnosed with a continuously elevated serum creatinine level of 1.3 mg/dL or greater 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 case of an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is performed in case of a positive exercise electrocardiogram. Eventually, CHD was diagnosed either angiographically or with the Doppler

Results

Table 1 presents the bio-demographic characteristics of the 500 patients attending primary healthcare centers (PHC) in Tabuk City, Saudi Arabia. Regarding age, 44.4% (n=222) were younger than 50 years, 13.8% (n=69) were exactly 50 years old, and 41.8% (n=209) were older than 50 years. The majority were females (71.2%, n=356), while males constituted 28.8% (n=144). Most participants were Saudi nationals (92.4%, n=462). Regarding educational level, a large proportion were university graduates (72.6%, n=363), followed by those with secondary education (14.2%, n=71), below secondary (10.6%, n=53), and no formal education (2.6%, n=13). As for employment status, 50.2% (n=251) were employees or self-employed, 28.4% (n=142) were retired, and 21.4% (n=107) were not working, or were students.

When asked about prior Varicella (chickenpox) infection, 40.0% (n=200) reported having had the disease, whereas 60.0% (n=300) had not. Among those who had Varicella, 58.0% (n=116) contracted it in childhood, 22.0% (n=44) during adolescence, 13.0% (n=26) as adults, and 7.0% (n=14) did not recall the timing. Regarding Varicella vaccination, 38.4% (n=192) reported being vaccinated, 23.6% (n=118) were not, and 38.0% (n=190) did not remember. Among those vaccinated, 44.1% (n=156) received it in childhood, 4.0% (n=14) during adolescence, 3.1% (n=11) as adults, and 48.9% (n=173) could not recall when. Finally, only 5.8% (n=29) of the participants reported a previous episode of shingles (Herpes Zoster), while the vast majority (94.2%, n=471) had not experienced it.

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 endpoints 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)

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

Discussion

Excess weight may be the most common cause of vasculitis, and actually the term should be replaced with excess fat tissue in the body. Probably, obesity is one of the terminal endpoints of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide little benefit either to reverse obesity or to prevent its endpoints. Excess fat tissue leads to a chronic and low-grade inflammation on vascular endothelium, and risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess fat tissue (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 the 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 tissue 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 tissue 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 tissue 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 illnesses in human being (28).

Smoking may be the second most common cause of vasculitis all over the world. Probably, it causes a systemic inflammation on vascular endothelium terminating with an atherosclerosis-induced multiorgan failures in early decades of life (29). Its atherosclerotic effect is obvious in the 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 characteristic features are inflammation, fibrosis, and narrowing and occlusions of arteries and veins. Claudication is the most common symptom with a severe pain caused by insufficient blood supply in feet and hands, particularly with 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 terminal endpoints. 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 required since 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. 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 example, smoking is usually associated with depression, irritable bowel syndrome (IBS), chronic gastritis, hemorrhoids, and urolithiasis with several underlying mechanisms (40). First of all, smoking may also have some antidepressive properties. Secondly, smoking-caused vascular inflammation may disturb epithelial functions for absorption and excretion in the gastrointestinal (GI) and genitourinary (GU) tracts (41). Thirdly, diarrheal losses-caused urinary changes may cause urolithiasis (42). Fourthly, smoking-caused sympathetic nervous system activation may induce motility problems in the GI and GU tracts terminating with IBS and urolithiasis. Finally, immunosuppression secondary to smoking-caused vascular inflammation may terminate with the GI and GU tract infections inducing urolithiasis because some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits. Actually, 10% of urinary stones are struvite stones those 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 IBS ($p<0.01$) (40).

Together with the stroke, CHD is the other final cause of death in human being. The most common underlying cause is the disruption of atherosclerotic plaques in an epicardial coronary artery, which leads to a clotting cascade. The plaques are the gradual and unstable collection of lipids, fibrous tissue, and white blood cells (WBC), especially the macrophages in arterial walls in decades of life. 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, 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 significant 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 tissue 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 endpoints 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 or 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 endpoint 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 the crises. Actually, each crisis may complicate with the following crises by leaving significant sequelaes on the capillary endothelial system all over the body. After a period of time, the sequelaes may terminate with sudden multiorgan failures and death during a final acute painful crisis that may even be silent, clinically. Similarly, after a 20-year experience on such patients, the deaths seem sudden and unexpected events in the 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 kept just for acute events and 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. Terminally, cost of the simple and repeated transfusions on insurance system is much lower than the exchange that needs trained staff and additional devices. On the other hand, pain is the result of complex and poorly understood interactions between 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 endpoints 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 death that may develop secondary to multiorgan failures on the chronic atherosclerotic background of the SCD.

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). 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 was the 58th most commonly prescribed medication in the United States in 2020. Similar with aspirin, warfarin does not have any effect on blood viscosity. It can prevent formation of blood clots and reduce the risk of thromboembolism. Warfarin is the best suited for anticoagulation in areas of slowly flowing blood such as veins and the pooled blood behind artificial and natural valves and dysfunctional cardiac atria. It is commonly used to prevent blood clots formation as in DVT and pulmonary embolism, and to protect against stroke in atrial fibrillation (AF), valvular heart disease, and 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 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. 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, 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). Thirteen publications from 11 cohorts including more than 48.500 patients with more than 11.600 warfarin users were included in the meta-analysis in which 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) anticoagulated either with warfarin or dabigatran had lower risk of recurrent venous thrombotic events (VTE), and the risks of bleeding were similar in both regimens (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 use of low-dose warfarin is highly effective and safe 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 similar in both groups ($p>0.05$) (83). Additionally, very-low-dose warfarin was safe and effective for prevention of thromboembolism in metastatic breast cancer in which the average daily dose was 2.6 mg, and the mean INR value 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, infection, inflammation, medical or surgical emergency, 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 in the SCD (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 endothelial inflammation and to prevent thromboembolic events in them (89).

COPD is the third leading cause of death in human being (90, 91). Aging, smoking, alcohol, male gender, excess fat tissue, chronic inflammation, prolonged infection, 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 endpoint 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 endpoint 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 or 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 or 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 endpoints 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).

Together with the CHD, stroke is the other final cause of death, and it develops as an acute thromboembolic event on the chronic atherosclerotic background. Aging, male gender alone, smoking, alcohol, excess fat tissue, chronic inflammatory or infectious processes, cancers, and excessive stress 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 cases with the SCA and higher WBC counts (115). Sickling-induced capillary endothelial damage, activations of WBC, PLT, and coagulation system, and hemolysis may terminate with chronic capillary endothelial damage, inflammation, edema, and fibrosis (116). Probably, stroke does not have a macrovascular origin in the SCD, and diffuse capillary endothelial inflammation, edema, and fibrosis may be much more significant. Infection, inflammation, medical or surgical emergency, and emotional stresses may precipitate stroke by increasing basal metabolic rate and sickling. Decreased stroke with hydroxyurea can also suggest that a significant proportion of cases is developed due to the increased WBC and PLT counts-induced an accelerated capillary endothelial edema in the SCD (117).

Acarbose, a pseudotetrasaccharide, is a natural microbial product of Actinoplanes strain SE 50. It is an alpha-glucosidase inhibitor. It binds to oligosaccharide binding site of alpha-glucosidase enzymes in the brush border of the small intestinal mucosa with a dose-dependent manner,

reversibly and competitively. It inhibits glycoamylase, sucrase, maltase, dextranase, and pancreatic alpha-amylase. It has little affinity for isomaltase but does not have any effect on beta-glucosidases such as lactase. As a result, it delays the intestinal hydrolysis of oligo- and disaccharides mainly in the upper half of the small intestine. By this way, the absorption of monosaccharides is delayed, and transport into the circulation is interrupted. Actually, it does not have any direct effect on absorption of glucose. Acarbose should be taken with the first bite of the meal, and its effects may prolong up to 5 hours. The suppression of alpha-glucosidases is persistent with long-term use. Up to now, acarbose failure has not been seen. Its usage results with carbohydrates appearing in the colon where bacterial fermentation occurs, accounting for the frequency and severity of GI adverse effects such as flatulence, loose stool, and abdominal discomfort (118). If started with a lower dose and titrated slowly, it tends to cause tolerable GI side effects (119). Long-term use increases colonic bacterial mass that of lactobacteria in particular. The finally impaired carbohydrate absorption, increased bacterial carbohydrate fermentation, and fecal acidification mimic effects of lactulose in cirrhosis and portosystemic encephalopathy. So acarbose has a favourable therapeutic profile for the long-term use even in cirrhosis. Similarly, observed changes in bacterial flora and decreased stool pH and beta-hydroxybutyrate may be associated with anti-proliferative effects on the epithelial cells of colon that may potentially decrease the risk of carcinogenesis. After oral administration, less than 2% of the unchanged drug can enter into the circulation. Thus there is no need for dosage adjustment in mild renal insufficiency. After a high carbohydrate meal, acarbose lowers the postprandial rise in blood glucose by 20% and secondarily FPG by 15% (120). Similarly, it lowers fasting and postprandial insulin levels. The initial improvement in blood glucose tends to be modest, but efficacy steadily improves with the long-term use, and is maintained over several years. Its beneficial effects on serum lipids were also documented with a dose-dependent manner (120), since dietary carbohydrates are key precursors of lipogenesis, and insulin plays a central role for postprandial lipid metabolism. Carbohydrate-induced postprandial triglyceride synthesis is reduced for several hours, so acarbose lowers plasma triglyceride levels (120). The same beneficial effect is also seen in non-diabetic patients with hypertriglyceridemia, and acarbose reduced LDL significantly, and HDL remained as unchanged in hyperinsulinemic and overweight patients with impaired glucose tolerance (IGT) (121). Significantly elevated ursocholic acids in the stool appear to be the additive endpoint of a decreased rate of absorption and increased intestinal motility due to the changes of intestinal flora. Acarbose may lower serum LDL via increased fecal bifido bacteria and biliary acids. Acarbose together with insulin was identified to be associated with a greater improvement in the oxidative stress and inflammation in type 2 DM (122). Probably, acarbose improves release of glucagon-like peptide-1, inhibits PLT activation, increases epithelial nitrous oxide synthase activity and nitrous oxide concentrations, promotes weight loss, decreases BP, and eventually prevents endothelial dysfunction (120). So it prevents stroke-like atherosclerotic endpoints of excess weight even in the absence of IGT or DM (123, 124). Although some authors reported as opposite (125), it should be used as the first-line antidiabetic agent together with metformin. Based on more than 40 years of clinical use, numerous studies did not show any significant toxicity or loss of appetite (126).

As a conclusion, hardened RBC-induced capillary endothelial damage initiated at birth terminates with multiorgan failures in early decades of life in the SCD. Excess fat may be much more important than smoking and alcohol for atherosclerosis since excess weight-induced DM is the most common cause of the CRD. The efficacy of acarbose to lower blood glucose by preventing breakdown of starch into sugar in the small intestine is well-known. Since acarbose is a safe, cheap, oral, long-term used, and effective drug for excess weight, it should be prescribed in prevention of stroke, particularly after the age of 50 years even in cases with normal weight because there are nearly 19 kg of excess fat even between the lower and upper borders of normal weight in adults.

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Prevalence of Vitamin D Deficiency and Low Energy Fractures: a Cross-Sectional Study

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Abstract

Background: Vitamin D plays a critical role in bone mineralization and musculoskeletal health. In regions such as Hail, Saudi Arabia, factors like sun exposure habits, clothing practices, and lifestyle may influence vitamin D levels and fracture risks. This study investigates the association between vitamin D levels, sun exposure patterns, and fracture characteristics among residents in the Hail region.

Methods: A cross-sectional study was conducted among 2,951 residents of the Hail region. Participants completed a structured questionnaire covering fracture history, sun exposure frequency and duration, clothing coverage, and vitamin D testing and levels. Among them, 1,342 individuals reported a history of bone fractures confirmed by X-ray. Descriptive statistics and chi-square tests were used to assess associations between variables using SPSS version 28, with significance set at $p < 0.05$.

Results: Out of 2,951 participants, 45.5% reported a history of confirmed bone fractures. The majority occurred between ages 6–10 years (30.0%), with falls being the most common cause (70.0%). Upper extremities were the most frequently fractured site (40.1%). Most participants with fractures had limited sun exposure; 65.1% for less than 10 minutes per day, and only 15.0% had daily exposure. Full body coverage was reported by 45.0%. Among those with fractures, 55.0% had never tested their vitamin D levels, and 66.7% of those tested had low levels (20–40 ng/mL). Morning sun exposure correlated significantly with normal vitamin D levels (75.0%), while full-body coverage and midday/sunset exposure were associated with deficiency ($p < 0.001$). Participants with normal vitamin D levels experienced fractures primarily between ages 6–10 and more than six years ago, while those with low vitamin D had broader and more recent fracture histories. Low vitamin D levels were significantly linked to lower limb fractures and falls, whereas normal levels correlated with upper limb and exercise-related fractures.

Conclusion: This study highlights a significant association between low vitamin D levels and recent, lower extremity fractures in the Hail population, especially among individuals with poor sun exposure and full-body clothing. Routine vitamin D testing and public awareness campaigns promoting early morning sun exposure and bone health education are recommended to reduce fracture risk in the region.

Keywords
Vitamin D deficiency, bone fractures, sun exposure, Saudi Arabia, orthopedic health, Hail region

Introduction

Bone fractures remain a significant global health concern, carrying substantial personal, societal, and economic consequences. This burden is particularly evident in individuals affected by osteoporosis or chronic conditions that compromise bone integrity, increasing their susceptibility to fractures from minor or low-impact trauma. Such injuries often result in diminished mobility, loss of independence, a decline in quality of life, and increased healthcare utilization and caregiver demands (1). While numerous studies have explored fracture epidemiology, many have not sufficiently examined the modifiable risk factors underlying these events. In response to this gap, large-scale epidemiological efforts such as the Global Burden of Disease (GBD) study have played a critical role in quantifying the prevalence, incidence, and disability burden of fractures. The 2019 iteration of the GBD offers comprehensive data across various age groups and regions, providing valuable insights to inform prevention and management strategies on national and global scales (2). In Saudi Arabia, particularly Hail region there remains a notable deficiency in research addressing the relationship between low-energy fractures and vitamin D deficiency, despite the well-established role of vitamin D in calcium homeostasis and bone metabolism (3,4). Low serum vitamin D levels are known to impair bone mineralization, potentially increasing fracture risk, particularly in populations already predisposed due to age, comorbidities, or limited sun exposure. Hip fractures are among the most serious types of fragility fractures, with studies indicating that up to 30% of affected individuals may die within a year of the injury, while many survivors endure long-term functional impairment and reduced quality of life (5,6). The World Health Organization defines fragility fractures as those occurring from minimal trauma—commonly in older adults—and attributes their rising incidence to factors such as aging populations, diabetes, obesity, polypharmacy, and social or environmental influences (7). Projections from high-income countries illustrate the scale of this issue. For example, in Sweden, the population aged 50 and above is expected to grow by 18% between 2010 and 2025, with a predicted 26% rise in fracture incidence during the same period (8). Epidemiological data consistently identify the distal radius, hip, ankle, and proximal humerus as the most frequently fractured sites, with distal radius fractures accounting for a considerable proportion in both pediatric and geriatric populations (9). This trend has been attributed to increased participation in physical activities among children and greater mobility in the elderly, alongside improved diagnostic practices. In Saudi Arabia, national estimates suggest that the incidence of hip fractures among adults aged 50 and older could increase nearly sevenfold by 2050 (10). While the overall risk of osteoporotic fractures may currently be lower than in some neighboring countries, this has been partly attributed to elevated all-cause mortality in the elderly population (11). Nevertheless, the escalating burden of fragility fractures underscores the urgent need for targeted prevention, including improved screening for risk factors such as vitamin D deficiency. This study aims to investigate the association between vitamin D deficiency and low-energy fractures in the Hail region of Saudi Arabia, where data remain limited. By better understanding this relationship, the research seeks to contribute to the development of evidence-based public health initiatives focused on fracture prevention and bone health optimization across the population.

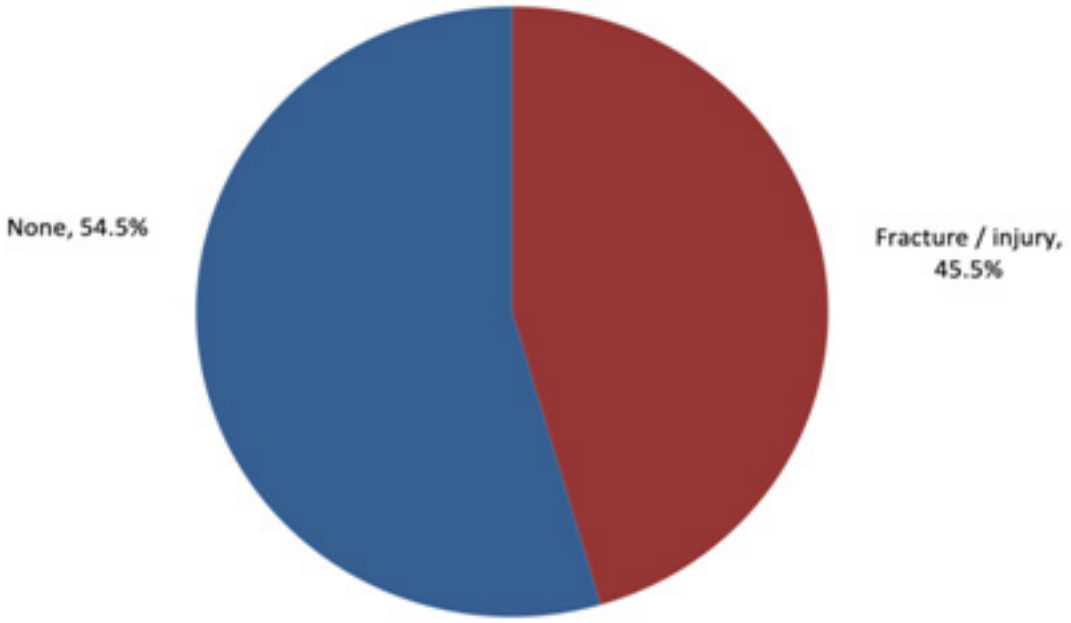
Methodology

This cross-sectional study was conducted using a structured, self-administered electronic questionnaire designed to collect information on demographics, fracture history, vitamin D status, lifestyle, and dietary habits. The questionnaire was previously validated and available in Arabic. The target population included residents of Hail Province, Saudi Arabia, from both urban and rural settings. Participants were selected from the general population, regardless of gender or nationality, provided they were currently living in the Hail region. Individuals who were not residing in Hail were excluded from participation. The sample size was calculated using the Raosoft sample size calculator, assuming a 95% confidence level and a 5% margin of error. Based on these parameters, a total of 3286 responses were deemed sufficient for statistical analysis and generalizability to the local population. After data collection, responses were reviewed for completeness, then coded and entered into IBM SPSS Statistics (version 22) for analysis. Descriptive statistics, including frequencies and percentages, were used to summarize all variables such as age, gender, fracture site and type, associated risk factors, and vitamin D-related behaviors (e.g., supplement use, sun exposure). To examine associations between vitamin D deficiency and the occurrence of low-energy fractures, inferential statistical tests were applied. Cross-tabulation was used to assess relationships between categorical variables, while Pearson's chi-square test (or exact probability tests when cell counts were small) was used to evaluate statistical significance. A p-value of less than 0.05 was considered statistically significant in all analyses.

Results

A total of 2,951 participants were included in the study. When asked whether they had ever experienced a bone fracture or injury (such as a hairline fracture) that was diagnosed and confirmed by X-ray, 1,342 participants (45.5%) reported having such a history, while 1,609 participants (54.5%) reported no history of confirmed bone fractures (Figure 1).

Figure 1. Participant History of X-ray Confirmed Bone Fractures in Hail Region, Saudi Arabia (N=2951)



Among the 1342 participants who reported having experienced a confirmed bone fracture in the Hail region, the majority had their fractures between the ages of 6–10 years (402; 30.0%), followed by 16–18 years (268; 20.0%), and 3–5 years and 11–15 years (each with 202 cases; 15.1%). As for the approximate duration of injury, the highest proportion of participants (470; 35.0%) reported having their fracture 6–10 years ago, followed by 1–3 weeks (268; 20.0%) and 1–2 years or less than a week (each around 10.0%). Fewer participants reported injuries that occurred 4–6 months ago (134; 10.0%), 1–3 months (67; 5.0%), 3–5 years (67; 5.0%), or 6–11 months ago (67; 5.0%). When examining the cause of fractures, falls were the most common cause, reported by 940 participants (70.0%), followed by injuries sustained while exercising (134; 10.0%), traffic accidents (134; 10.0%), objects falling on the body (67; 5.0%), and fights (67; 5.0%). About the site of fracture, the most frequently affected areas were the bones of the upper extremities including the humerus, ulna, and elbow reported by 538 participants (40.1%), followed by bones of the leg and foot (469; 34.9%). Fractures in the carpal bones (134; 10.0%), lower extremities such as the thigh and knee (134; 10.0%), and specifically the patella (67; 5.0%) were less common.

Table 1. Characteristics of Bone Fractures among Affected Participants in Hail Region, Saudi Arabia (N=1342)

Items	No	%
Age at fracture time		
Less than 1 year	67	5.0%
1-2 years	67	5.0%
3-5 years	202	15.1%
6-10 years	402	30.0%
11-15 years	202	15.1%
16-18 years	268	20.0%
19-25 years	134	10.0%
Approximate duration of injury?		
Less than 1 week	134	10.0%
1-3 weeks	268	20.0%
1-3 months	67	5.0%
4-6 months	134	10.0%
6-11 months	67	5.0%
1-2 years	135	10.1%
3-5 years	67	5.0%
6-10 years	470	35.0%
The reason for fracture		
Fall	940	70.0%
While exercising	134	10.0%
Traffic accident	134	10.0%
An object falling on the body	67	5.0%
During fight	67	5.0%
Site of fracture		
In the bones of the upper extremities (including the humerus, ulna and elbow)	538	40.1%
In the bones of the leg and foot (including the ankle, tibia, fibula, and toes)	469	34.9%
In the carpal bones (including the fingers and wrist)	134	10.0%
In the lower extremities (including the thigh and its joint, the knee, and the patella, commonly known as the kneecap)	134	10.0%
Patella	67	5.0%

Among the 1,342 participants who had experienced bone fractures in the Hail region (Table 2), the majority reported limited sun exposure. Considering the frequency, nearly half (670 participants; 49.9%) stated they were exposed to sunlight "sometimes" during the week, while 25.0% (336) reported rare exposure and 10.1% (135) were very rarely exposed. Only 15.0% (201) had daily sun exposure. Regarding duration, a significant proportion (873 participants; 65.1%) were exposed to sunlight for less than 10 minutes per day, while 402 (30.0%) reported exposure for 10–30 minutes, and only a small minority (67; 5.0%) had exposure for more than 30 minutes. As for the time of day, 603 participants (44.9%) were exposed to sun in the morning (before 10 AM), followed by 538 (40.1%) around midday, and 201 (15.0%) at sunset. When asked about clothing coverage, 604 participants (45.0%) reported covering their entire body, while 537 (40.0%) did not. A further 201 (15.0%) did not respond to this question.

Table 2. Patterns of Sun Exposure among Participants who Experienced Bone Fracture in the Hail Region, Saudi Arabia (N = 1342)

Sun exposure	No	%
Frequency of sun exposure /week		
Very rarely	135	10.1%
Rarely	336	25.0%
Sometimes	670	49.9%
Daily	201	15.0%
Sun exposure duration / time		
Less than 10 minutes	873	65.1%
10-30 minutes	402	30.0%
More than 30 minutes	67	5.0%
Approximate time of sun exposure?		
Morning (before 10 am)	603	44.9%
In the middle of the day (noon)	538	40.1%
At sunset	201	15.0%
Do you cover your whole body?		
Yes	604	45.0%
No	537	40.0%
No response	201	15.0%

Table 3 shows vitamin D assessment among 1,342 participants who had experienced bone fractures in the Hail region. Less than half (604 participants; 45.0%) reported that they had previously tested their vitamin D levels, while the majority (738; 55.0%) had never undergone vitamin D testing. Of those who had been tested, the time since the most recent test varied: about 33.3% (201 participants) had their vitamin D levels assessed 1–3 months ago, and a similar proportion (33.4%; 202 participants) had tested 3–5 years ago, suggesting that for many individuals, testing may not be recent enough to reflect current status. Smaller proportions reported testing done less than 1 week ago (67; 11.1%), 4–6 months ago (67; 11.1%), or 1–2 years ago (67; 11.1%). As for the reported levels, the majority (336 participants; 55.6%) indicated that their vitamin D levels were low (20–40 ng/mL). Another 11.1% (67) knew their levels were low but could not recall the exact values. Only 33.3% (201 participants) reported having normal vitamin D levels (41–80 ng/mL).

Table 3. Vitamin D Testing History and Reported Levels among Participants with Bone Fractures in the Hail Region (N = 1342)

Vitamin D	No	%
Have you had your vitamin D level tested?		
Yes	604	45.0%
No	738	55.0%
How long ago was your last test?		
Less than 1 week	67	11.1%
1-3 months	201	33.3%
4-6 months	67	11.1%
1-2 years	67	11.1%
3-5 years	202	33.4%
Level of assessed vitamin D		
Normal (41 to 80 ng/mL)	201	33.3%
Low (20 to 40 ng/mL)	336	55.6%
Low but do not remember value	67	11.1%

Table 4 assessed the relationship between sun exposure and vitamin D levels among participants in Hail, Saudi Arabia (N=1342). Regarding the frequency of sun exposure per week, individuals who reported being exposed to the sun "sometimes" had the highest proportion of normal vitamin D levels (60.0%), whereas all of those with "very rare," "rare," or "daily" exposure had low vitamin D levels, indicating a possible inconsistency in the effectiveness of sun exposure when it is either too infrequent or potentially at times when synthesis is suboptimal. For duration of sun exposure, participants exposed for less than 10 minutes daily showed a nearly equal distribution between normal (49.9%) and low (50.1%) vitamin D levels. In contrast, all of those exposed for 10–30 minutes had low vitamin D levels. When examining the approximate time of sun exposure, morning exposure (before 10 am) was significantly associated with normal vitamin D levels (75.0%), while noon and sunset exposure were linked to 100% low vitamin D levels. Regarding clothing habits, all participants who reported covering their entire body had low vitamin D levels (100%), while those who did not cover completely showed a better profile, with 39.9% having normal vitamin D. Also all of those who gave no response had normal levels, which may reflect a reporting or categorization bias. All exposure data showed a significant association with p-value less than 0.05.

The analysis of the relationship between vitamin D levels and bone fracture characteristics, several statistically significant associations were reported. With regard to age at the time of fracture, all participants with normal vitamin D levels (100.0%) reported having had fractures between the ages of 6–10 years, while no participants with normal vitamin D levels reported fractures at younger or older age ranges. In contrast, those with low vitamin D levels experienced fractures across a broader range: 33.5% at ages 3–5 years, 33.3% at 16–18 years, and 16.6% each at 11–15 and 6–10 years (p = 0.001). Regarding the approximate duration of injury, participants with normal vitamin D levels overwhelmingly reported fracture events that occurred 6–10 years ago (100.0%), whereas those with low vitamin D had a more recent history of injury, with 16.6% each reporting durations of less than 1 week, 1–3 months, 4–6 months, and 6–11 months, and 33.5% in the 6–10 year range (p = 0.001). As for the cause of fracture, 83.4% of those with low vitamin D reported falls as the main cause, compared to 66.7% among those with normal levels. Interestingly, 33.3% of participants with normal vitamin D levels reported fractures occurring while exercising, while none with low vitamin D did. Fractures due to fights were reported only among the vitamin D–deficient group (16.6%) (p = 0.001). Considering fracture sites, those with normal vitamin D were more likely to have injuries in the upper extremities (66.7%) and carpal bones (33.3%), while those with low vitamin D had a higher occurrence of fractures in the leg and foot bones (49.9%) and upper extremities (50.1%), with no reported carpal fractures (p = 0.001).

Table 4. The relation between Vitamin D Level and Participants' Sun Exposure in Hail, Saudi Arabia (N=1342)

Sun exposure	Level of assessed vitamin D				p-value
	Normal		Low		
	No	%	No	%	
Frequency of sun exposure /week					
Very rarely	0	0.0%	68	100.0%	
Rarely	0	0.0%	134	100.0%	.001*
Sometimes	201	60.0%	134	40.0%	
Daily	0	0.0%	67	100.0%	
Sun exposure duration / time					
Less than 10 minutes	201	49.9%	202	50.1%	.001*
10-30 minutes	0	0.0%	201	100.0%	
Approximate time of sun exposure?					
Morning (before 10 am)	201	75.0%	67	25.0%	.001*
In the middle of the day (noon)	0	0.0%	202	100.0%	
At sunset	0	0.0%	134	100.0%	
Do you cover your whole body?					
Yes	0	0.0%	201	100.0%	.001*
No	134	39.9%	202	60.1%	
No response	67	100.0%	0	0.0%	

P: Exact Probability test
* P < 0.05 (significant)

Table 5. The relation between Vitamin D Level and Bone Fracture Data in Hail, Saudi Arabia (N=1342)

Factors	Level of assessed vitamin D				p-value
	Normal		Low		
	No	%	No	%	
Age at fracture time					
3-5 years	0	0.0%	135	33.5%	.001*
6-10 years	201	100.0%	67	16.6%	
11-15 years	0	0.0%	67	16.6%	
16-18 years	0	0.0%	134	33.3%	
Approximate duration of injury?					
Less than 1 week	0	0.0%	67	16.6%	.001*
1-3 months	0	0.0%	67	16.6%	
4-6 months	0	0.0%	67	16.6%	
6-11 months	0	0.0%	67	16.6%	
6-10 years	201	100.0%	135	33.5%	
The reason for fracture					
Fall	134	66.7%	336	83.4%	.001*
While exercising	67	33.3%	0	0.0%	
During fight	0	0.0%	67	16.6%	
Site of fracture					
In the bones of the upper extremities (including the humerus, ulna and elbow)	134	66.7%	202	50.1%	.001*
In the carpal bones (including the fingers and wrist)	67	33.3%	0	0.0%	
In the bones of the leg and foot (including the ankle, tibia, fibula, and toes)	0	0.0%	201	49.9%	

P: Exact Probability test
* P < 0.05 (significant)

Discussion

This study assessed the relationship between vitamin D deficiency and low-energy fractures in the Hail region of Saudi Arabia, involving a large sample of participants. A significant number of individuals reported a history of fractures, with most occurring during childhood and adolescence, particularly between ages 6–10 and 16–18. Falls were the leading cause of fractures, followed by exercise-related injuries and traffic accidents. The upper extremities, including the humerus and elbow, were the most commonly affected sites, while lower extremity fractures were less frequent.

These findings are consistent with previous research showing the high prevalence of fractures in younger age groups, likely due to increased physical activity and bone development phases. A study in Saudi Arabia by Al-Othman et al. (2012) found similar patterns, with fractures peaking in adolescence and being frequently linked to falls [12] and with other study by Abdulaziz et al. [13]. Additionally, the predominance of upper limb fractures is consistent with global data, as studies such as those by Agrawal et al. (2023) note that arms and wrists are more vulnerable to fractures during falls due to instinctive attempts to break impact [14] and also consistent with Arnold et al. [15], and Berry et al. [16].

As for vitamin D level, our study reveals important findings into vitamin D awareness and testing habits among individuals with a history of fractures in the Hail region. A concerning majority of participants had never been tested for vitamin D deficiency, indicating a defect in routine screening despite their fracture history. Among those who had been tested, many had not done so recently, with a significant portion (33.4%) last tested 3–5 years ago meaning their current vitamin D status remains uncertain. This delay in testing is a challenge, as vitamin D levels can vary over time due to factors such as seasonal changes, dietary intake, and sun exposure.

Most participants who knew their vitamin D levels reported insufficient or deficient levels (55.6% had levels between 20–40 ng/mL, while another 11.1% knew their levels were low but did not recall exact numbers). Only a third had normal levels (41–80 ng/mL). These findings match with previous research demonstrating widespread vitamin D deficiency in Saudi Arabia, particularly among populations with limited sun exposure or dietary intake of fortified foods. A study by Al-Daghri et al. (2017) found that over 60% of Saudi adults had insufficient vitamin D levels (<50 nmol/L), with women and younger individuals being particularly affected [17]. Similarly, a study by Elsammak et al. (2011) reported that 80% of healthy Saudi adults had vitamin D deficiency, likely due to cultural clothing practices, limited outdoor activity, and low dietary vitamin D intake [18].

The high prevalence of low vitamin D levels among fracture patients in this study supports existing evidence associating deficiency to poor bone health. A meta-analysis by Bischoff-Ferrari et al. (2009) found that individuals with low vitamin D levels had a significantly higher risk of fractures, particularly in weight-bearing bones, due to impaired calcium absorption and bone mineralization [19]. Another study by Holick (2007) highlighted that maintaining adequate vitamin D levels (≥30 ng/mL) is crucial for reducing fracture risk, especially in regions with limited sunlight exposure [20].

The study showed remarkable variations in fracture characteristics between individuals with normal and low vitamin D levels, underlining a potential association between vitamin D status and skeletal health. Participants with normal vitamin D experienced fractures exclusively between ages 6–10, while those with low vitamin D suffered fractures across a broader age spectrum, including early childhood (3–5 years) and adolescence (16–18 years). This pattern suggests a possible protective effect of sufficient vitamin D on bone integrity throughout different developmental stages. Fracture timing also varied; those with normal vitamin D typically had fractures that occurred 6–10 years ago, whereas individuals with low levels showed a higher incidence of recent fractures, including within the past year. Regarding fracture causes, falls were predominant in both groups but significantly more common among vitamin D–deficient participants. Also, exercise-related fractures were reported only in those with normal vitamin D possibly due to higher physical activity despite better bone strength. On the contrary, fractures from physical altercations were exclusive to the deficient group reflecting both reduced bone resilience and socio-behavioral factors. Differences were also evident in fracture locations. Participants with normal vitamin D levels sustained injuries primarily to the upper extremities and carpal bones, consistent with typical fall injuries. In contrast, those with low vitamin D showed a higher rate of leg and foot fractures mostly due to possible bone weakness in weight-bearing areas, with an absence of carpal fractures, supporting the hypothesis of altered fracture patterns linked to deficiency.

These findings are consistent with existing literature. LeBoff et al. (2022) observed higher rates of lower limb fractures in vitamin D–deficient individuals due to compromised bone mineralization and muscular function [21]. Similarly, Bischoff-Ferrari et al. (2010) demonstrated that vitamin D supplementation reduced nonvertebral fractures, particularly in those starting with low levels [19]. Age-specific trends observed in this study reflect those reported by Winzenberg et al. (2011), who found vitamin D deficiency associated with increased fracture risk in both children and adolescents [22]. Additionally, the prominence of falls simulate Sanders et al. (2010), who related deficiency to increased fall risk due to reduced muscle strength and balance [23].

The high rate of fractures in populations raises concerns about bone health and potential vitamin D deficiency, which is known to weaken bones and increase fracture risk. A study by Holvik et al. (2015) in Norway found that insufficient vitamin D levels were associated with higher fracture incidence in children and adolescents [24].

fracture incidence in children and adolescents [24]. Similarly, research by Munns et al. (2016) emphasized that vitamin D plays a crucial role in bone mineralization, and its deficiency can lead to rickets or osteomalacia, increasing susceptibility to fractures even from minor trauma [25].

In conclusion, this study showed association between vitamin D status, sun exposure habits, and bone fracture history in the Hail region. A significant portion of participants reported previous fractures, most commonly during childhood. Falls were the leading cause, and the upper limbs were the most frequently affected sites. Among those with a history of fractures, limited sun exposure was common, and the majority had either never tested their vitamin D levels or had low results when tested. Individuals with normal vitamin D levels tended to experience fractures during a narrower age window and had less recent injuries mainly due to stronger bone health. On the other hand, vitamin D–deficient individuals showed broader and more recent fracture patterns, potentially reflecting increased susceptibility or delayed recovery. Sun exposure patterns significantly influenced vitamin D levels. Morning exposure was more likely to be associated with adequate vitamin D, whereas exposure at midday or sunset and full-body coverage were linked to deficiency. Increasing public knowledge on the importance of vitamin D and its role in bone health is highly recommended. Additionally enhancing regular exposure to early morning sunlight as a safe and effective way to support vitamin D synthesis is mandatory. Introduce routine vitamin D testing, particularly for those with limited sun exposure or fracture history is also recommended.

Conclusion and Recommendations

In conclusion, this study showed association between vitamin D status, sun exposure habits, and bone fracture history in the Hail region. A significant portion of participants reported previous fractures, most commonly during childhood. Falls were the leading cause, and the upper limbs were the most frequently affected sites. Among those with a history of fractures, limited sun exposure was common, and the majority had either never tested their vitamin D levels or had low results when tested. Individuals with normal vitamin D levels tended to experience fractures during a narrower age window and had less recent injuries mainly due to stronger bone health. On the other hand, vitamin D–deficient individuals showed broader and more recent fracture patterns, potentially reflecting increased susceptibility or delayed recovery. Sun exposure patterns significantly influenced vitamin D levels. Morning exposure was more likely to be associated with adequate vitamin D, whereas exposure at midday or sunset and full-body coverage were linked to deficiency. Increasing public knowledge on the importance of vitamin D and its role in bone health is highly recommended. Additionally enhancing regular exposure to early morning sunlight as a safe and effective way to support vitamin D synthesis is mandatory. Introduce routine vitamin D testing, particularly for those with limited sun exposure or fracture history is also recommended.

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Hypertension risk stratification: Quality Improvement Project

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Abstract

Hypertension is a key risk factor for cardiovascular disease, yet initial assessments often fall short of guideline standards. This quality improvement project audited compliance with NICE guideline [NG136] in a large Nottingham general practice and evaluated the impact of introducing an electronic checklist.

Key words: Hypertension, quality improvement, NICE guidelines, risk stratification

Background

Hypertension, defined as a persistent elevation in systolic (≥140 mmHg) or diastolic (≥90 mmHg) blood pressure, remains one of the most prevalent and modifiable risk factors for cardiovascular disease (CVD) worldwide (World Health Organisation, 2021). It is primarily classified as either primary (essential) hypertension, which accounts for approximately 85% of cases with no identifiable cause, or secondary hypertension, which is attributed to underlying medical conditions (Ferri F, 2019).

Globally, one in four adults has hypertension, a figure expected to rise to over 1.5 billion by 2025 (World Health Organisation, 2021). In England alone, 26.2% of adults (11.8 million people) were estimated to have hypertension in 2017, with a significant proportion remaining undiagnosed (Public Health England, 2020). Hypertension contributes substantially to cardiovascular morbidity and mortality by causing damage to target organs such as the heart, kidneys, retina, and brain. The burden of CVD in England was reflected in an estimated healthcare cost of £7.4 billion in 2019/20, driven by over one million hospital admissions and 5.5 million bed days (Ahmed S et al, 2023).

Preventive strategies focusing on modifiable risk factors are essential. The National Institute for Health and Care Excellence (NICE) highlights the importance of early identification and management of CVD risk factors and target organ damage at the point of hypertension diagnosis (NICE guideline [NG136], 2019). Timely assessment enables stratification and appropriate therapeutic interventions, improving long-term outcomes.

Aims and Objectives

This quality improvement project aimed to assess compliance with NICE guideline in the evaluation of cardiovascular risk and target organ damage in newly diagnosed hypertensive patients. The audit specifically sought to:

- Evaluate the proportion of patients who underwent guideline-recommended assessments.
- Identify areas for improvement in clinical performance.
- Implement a hypertension checklist template within the electronic medical record system to enhance compliance.
- Re-evaluate compliance post-intervention to measure impact.

Standards Used

This audit was based on NICE Guideline [NG136]: Hypertension in Adults: Diagnosis and Management.

Key standards for newly diagnosed hypertensive patients include:

1. QRISK calculation to estimate 10-year cardiovascular risk.
2. Urinalysis for proteinuria and microscopic haematuria.
3. Blood tests for HbA1c, renal function (creatinine, eGFR, electrolytes), and lipid profile.
4. 12-lead ECG to detect left ventricular hypertrophy, arrhythmias, or ischaemic changes.
5. Fundoscopic examination to assess for hypertensive retinopathy.

Patients newly diagnosed with stage 1 hypertension should start antihypertensive medication if their QRISK score is 10% or higher or if there's evidence of target organ damage. NICE guidelines also recommend considering statin therapy for primary prevention of cardiovascular disease when the QRISK score is 10% or more (NICE guideline [NG238], 2023).

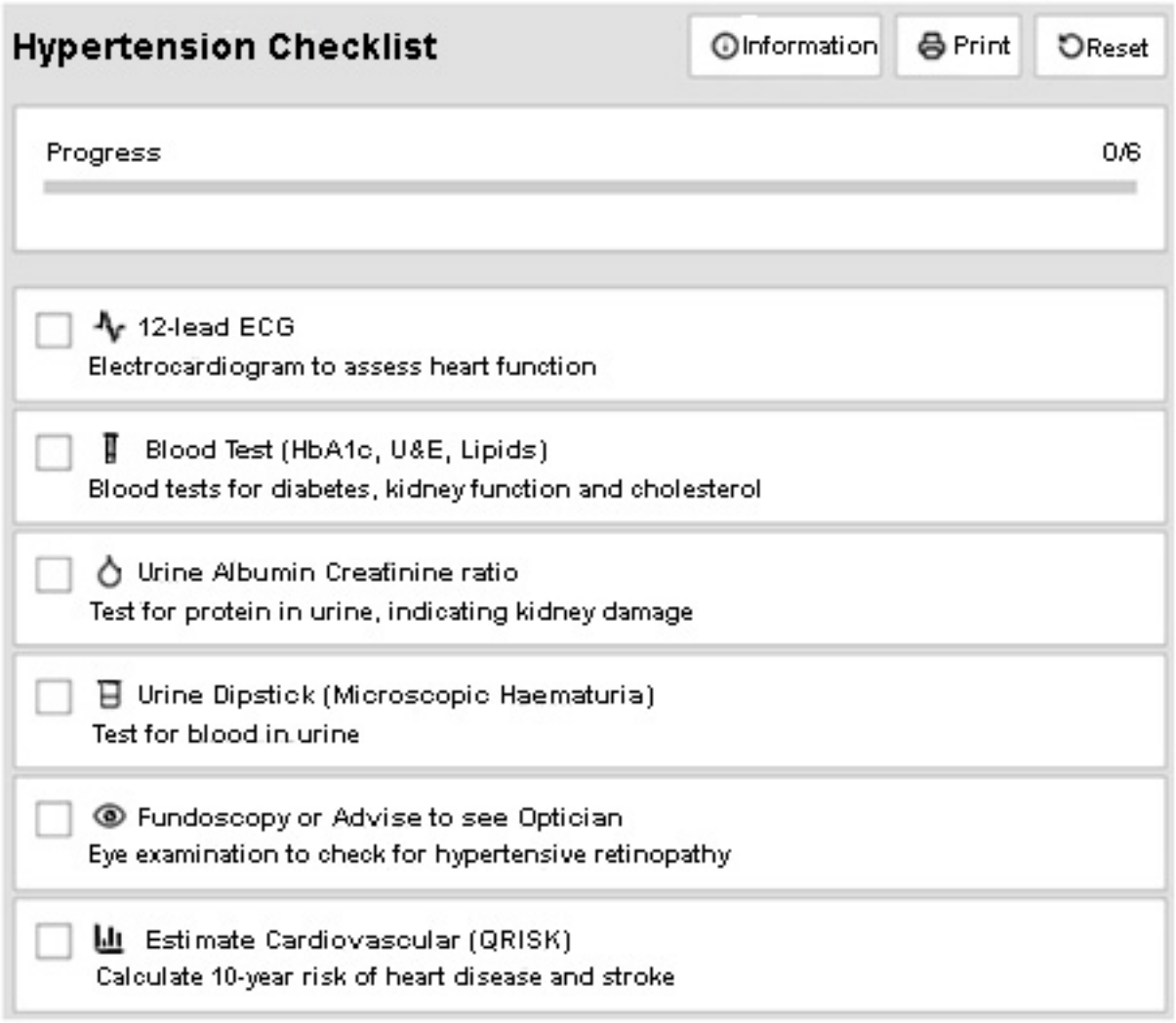
Method

A retrospective audit was conducted using SystmOne, the primary electronic health record system at a large Nottingham general practice. A search identified newly diagnosed hypertensive patients between May 2018 and May 2019. Patients with existing diagnoses of chronic kidney disease (CKD), diabetes mellitus, coronary artery disease, or cerebrovascular disease were excluded to isolate new hypertension cases.

From the eligible patients identified, a random sample of twenty patient records were randomly selected and reviewed to assess compliance with NICE guidelines. Following the initial audit, results were disseminated to clinical staff, and an intervention was implemented. With help from the IT department a hypertension checklist template was introduced into SystmOne (Figure 1). This template was triggered by hypertension-related Read codes or elevated BP readings. The template prompted clinicians to complete relevant assessments and remained active until all checklist items were completed. Nurses and healthcare assistants were encouraged to opportunistically collect urine samples during routine blood tests or ECG appointments.

Twelve months later, a second retrospective audit was conducted using the same methodology and sample size to assess changes in compliance.

Figure 1: Hypertension checklist template



Results

First Audit cycle (Pre-Checklist Implementation) – Table 1

Out of a practice population of 15,045, 1,845 (12.3%) were diagnosed with hypertension between May 2018 and May 2019. After excluding patients with comorbidities, 846 were identified with isolated hypertension. A sample of 20 patients was reviewed:

- Blood tests: 55% compliance.
- ECG: 35%.
- Urinalysis (dipstick): 30%.
- Urine microalbumin: 25%.
- Fundoscopy: 0%.
- QRISK2 score documented: 35%.
- Overall Compliance: 30%

Second Audit cycle (Post-Checklist Implementation) – Table 2

Another random sample of 20 newly diagnosed patients was assessed one year later:

- Blood tests: 100% compliance.
- ECG: 80%.
- Urinalysis (dipstick and microalbumin): 85%.
- Fundoscopy: 30% (note: no in-practice fundoscopy was performed; patients were referred to opticians).
- QRISK2 score documented: 75%.
- Overall compliance improved from 30% to 75.8% following the intervention.

Collective analysis demonstrated improvements across all assessment domains. Review of individual patient records revealed the early identification of several patients with significant findings, including pre-diabetic states, one confirmed diabetic patient, two patients with possible renal disease, and five individuals with QRISK scores exceeding 10%, prompting timely therapeutic

Table 1: Pre-Intervention analysis

CVD Risk Assessment ands target organ damage assessment within 6 months from diagnosis	Number of medical records analysed																			
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**Percentage**
Blood test - UE / HBA1c / Lipids	✓		✓				✓	✓		✓		✓		✓	✓		✓	✓		✓	55
12 lead ECG	✓		✓				✓	✓						✓	✓					✓	35
Urine dipstick for blood / protein					✓				✓					✓	✓			✓		✓	30
Urine microalbumin	✓		✓				✓	✓												✓	25
Fundoscopy / advice to see optician																					0
QRISK2 score calculated and recorded	✓		✓				✓	✓						✓	✓					✓	35
Overall																					30

Table 2: Post-intervention analysis

CVD Risk Assessment ands target organ damage assessment within 6 months from diagnosis	Number of medical records analysed																			
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**Percentage**
Blood test - UE / HBA1c / Lipids	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	100
12 lead ECG	✓	✓	✓	✓		✓	✓	✓		✓	✓	✓		✓	✓		✓	✓	✓	✓	80
Urine dipstick for blood / protein	✓	✓	✓	✓	✓		✓	✓		✓		✓	✓	✓	✓	✓		✓	✓	✓	85
Urine microalbumin	✓	✓	✓	✓	✓		✓	✓		✓		✓	✓	✓	✓	✓		✓	✓	✓	85
Fundoscopy / advice to see optician	✓		✓				✓	✓										✓	✓		30
QRISK2 score calculated and recorded	✓	✓	✓	✓	✓		✓	✓		✓		✓		✓	✓	✓		✓	✓	✓	75
Overall																					75.83

Discussion

There is a significant national initiative to enhance cardiovascular disease (CVD) management in primary care, with the ambitious goal of reducing heart attack and stroke mortality by 25% over the next decade (British Heart Foundation, 2024). The importance of this work cannot be overstated: in England alone, optimising blood pressure treatment for just 80% of diagnosed hypertensive patients could prevent over 17,000 cardiovascular events within three years, saving the NHS nearly £200 million (UCLPartners, 2025). Similarly, increasing statin treatment rates to 90-95% among CVD patients could prevent between 9,000-18,000 cardiovascular events over three years (ULCPartners, 2025). Early detection and comprehensive management of cardiovascular risk factors at the point of hypertension diagnosis represents a substantial opportunity to improve outcomes.

This audit revealed significant gaps in the initial assessment of newly diagnosed hypertensive patients, with only 30% overall compliance with NICE guidelines in the first cycle. Factors contributing to underperformance likely included time constraints, variability in clinician knowledge, lack of systematic prompts and limited awareness or application of guidelines.

Trainee GPs demonstrated higher adherence to guidelines, possibly due to longer consultation times and more recent training. Notably, fundoscopy was not performed in any case, reflecting practical limitations in primary care. Given the lack of strong evidence supporting routine fundoscopy in hypertension management (Van den Born BJ et al, 2005), advising patients to undergo optician assessments was considered a pragmatic alternative.

Following the introduction of a digital checklist, marked improvement was observed across all parameters. The checklist served as an effective reminder facilitating timely investigations, better documentation, and follow-up planning. Furthermore, the checklist promoted team-based care with nurses and healthcare assistants playing a key role in actively contributing to improved data collection, early detection of comorbidities and escalating abnormal findings. The checklist facilitated early detection of significant comorbidities including diabetes, renal disease, and elevated QRISK scores. This early identification enabled prompt therapeutic interventions, including appropriate antihypertensive medications and statins, potentially averting future cardiovascular events through timely risk factor management.

Conclusion

This quality improvement project demonstrates how a simple, systematic approach to hypertension assessment can significantly improve adherence to evidence-based guidelines and enhance early detection of cardiovascular risk. By implementing structured assessment tools in primary care, we can contribute meaningfully to national targets for CVD prevention while improving patient outcomes through comprehensive, evidence-based management that focuses on individual patient needs.

Suggestions

- Integration of clinical checklists: Embedding electronic templates into practice management systems can improve adherence to guidelines.
- Team-based care approach: Utilising the wider healthcare team, including nurses and HCAs, can enhance data collection and patient monitoring.
- Ongoing education: Regular training and updates for all clinicians on current guidelines is essential for maintaining standards of care.
- Fundoscopy recommendations: Until more practical solutions are available in primary care, referral to opticians should be standard practice for ocular assessment.
- Continual auditing: Regular audits should be performed to monitor progress, reinforce good practice, and guide future quality improvement initiatives.
- Scaling intervention: The successful checklist template should be disseminated to other practices within the region to support broader improvements in hypertension management.

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Maternal Awareness and Practice of Child Trauma, Saudi Arabia

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Abstract

Introduction: Childhood injury is a neglected public health problem with a sizeable burden on children's well-being and their families. Unintentional injury is one of the leading causes of mortality and morbidity among children.

Aim: The current study aimed to assess maternal knowledge and awareness about child trauma in Saudi Arabia.

Methods: A cross-sectional study was conducted on accessible and eligible mothers of children in a hospital from June 2024 to mid-august 2024. The study used a pre-structured questionnaire to collect bio-demographic data, child trauma history, and awareness about child trauma. The questionnaire's validity and reliability were assessed through a pilot study and expert review. The final questionnaire was distributed online to eligible participants until no new participants were obtained.

Results: A total of 351 (73.1%) mothers reported that at least one of their children was previously injured which was for 2-3 times among 160 (45.6%) of them, and for more than 3 times among 130 (37%). The most reported causes of injury were accidents (54.2%), fall from height (52%). As for awareness level, a total of 161 (33.5%) mothers had an overall good awareness about child trauma while the vast majority (66.5%) had poor awareness level.

Conclusion: The study found that most children experience childhood trauma, mainly contusions and fractures from falls or accidents. Mothers lack knowledge about first aid and preventive measures. Efforts to develop evidence-based educational programs are needed. National assessments are needed.

Keywords:
Child trauma, prevalence, mothers, awareness, practice, predictors, Saudi Arabia.

Introduction

Recently, many environmental and daily life factors have an impact on children's health now and in the future (1, 2). Because of their carelessness and lack of understanding about the nature of potentially harmful materials, children are more prone to trauma and injury (3). Children's injuries are particularly worrying (3, 4). In 2011, injuries claimed more than 630,000 lives among children (5). According to the Centers for Disease Control and Prevention (CDC), the leading cause of death from unintentional injuries was MVC followed by drowning, burns, and suffocation, whereas unintentional fall remains the most common cause for nonfatal injuries (6).

According to the GBD, unintentional injuries and transport injuries were two of the top 10 causes of death in Saudi Arabia (7). Injuries were the primary cause of the majority of avoidable fatalities among Saudi Arabian youngsters (82.5%) (8). MVC, which accounted for 60.6% of injury deaths, was most common among 13–18-year-olds. Drowning, which accounted for 13.4% of injury deaths, was most common among 6–12-year-olds (8).

Chronic health issues such as depression; asthma, heart disease, and obesity are linked to early and cumulative trauma exposure during critical developmental stages in children's lives (9-11). Research shows that childhood trauma has both immediate and long-term effects on childhood, adolescent, and early adult outcomes, in addition to intergenerational effects (12-15). As a result, treating childhood trauma has become increasingly important for public health (16).

Understanding and identifying the common behavioural and health requirements of young children who have suffered trauma is crucial for parents of young children as well as Early Childhood Education (ECE) caregivers (17). As awareness of this grows, attitudes toward how parents and ECE providers address the needs of their children may also change. According to Traub and Boynton-Jarrett (2017), this is a crucial initial step toward eventually changing parenting and caregiver behaviors to better fit with trauma informed care (18). The current study aimed to assess maternal awareness and practices about child trauma as well as to assess child trauma rate and associated risk factors among Saudi children.

Methodology

A descriptive cross-sectional study was conducted targeting all accessible and eligible mothers of children available in the study setting at the study hospital during the period from June 2024 to mid-august 2024. Mothers aged less than 18 years, those with no children less than 14 years and mothers who refused to participate or who did not complete the study questionnaire were excluded. Participants were recruited using convenience sampling method. A pre-structured questionnaire was used as the data collection tool. The study questionnaire included participants' bio-demographic data including age gender, education, employment and residence and the data of their children aged less than 14 years. Also, mother's residence area, type and level was assessed. The second section covered child trauma history among mothers including causes of trauma, types, frequency and sites of child trauma. The third section covered mother's awareness about child trauma with one or more correct answers per question and mothers' source of information about child trauma. The study questionnaire validity and reliability were assessed via pilot study on 25 participants and experts' review. Any modifications were applied until achieving the study questionnaire that was used. The tool reliability was 0.73 based on α-Cronbach's. The final study questionnaire was distributed online via social media platforms to all eligible participants by the study researchers and their families until no more new participants were obtained.

Data analysis

The data were collected, reviewed and then fed into Statistical Package for Social Sciences version 26 (SPSS: An IBM Company). All statistical methods used were two tailed with alpha level of 0.05 considering significance of P value less than or equal to 0.05. An overall awareness score was computed by summing the correct answers where correct answers were given 1-point score and 0 was given otherwise. Mothers with knowledge score less than 60% of the total correct answers were considered with poor awareness level while others with knowledge score of 60-100% were considered to have good awareness about child trauma. Descriptive analysis was done by prescribing frequency distribution and percentage for study variables including mother's personal data, residence data, employment, and their children's data. Also, child trauma data and its frequency, associated factors, and site of injury, besides maternal awareness and practice of Child Trauma, were tabulated while the overall awareness level and source of information were graphed. Cross tabulation was done for showing factors associated with mother's awareness about child trauma and factors associated with child trauma as reported by their mothers using Pearson chi-square test and exact probability test for small frequency distributions.

Results

A total of eligible 480 mothers completed the study questionnaire. Mothers' ages ranged from 20 to 57 years with a mean age of 31.5 ± 8.6 years old. A total of 321 (66.9%) were in an urban residence, 270 (56.3%) resided in rented units and 258 (53.8%) residents were on the ground floor. As for social status, 289 (60.2%) were married, 159 (33.1%) were separated and 32 (6.7%) were widows. Exactly 226 (47.1%) had secondary education, and 190 (39.6%) had university level of education. Considering employment, 225 (46.9%) were housewives, 124 (25.8%) worked in the governmental sector, and 99 (20.6%) in the private sector. Monthly income less than 5000 SR was reported among 192 (40%) of mothers while 130 (27.1%) had monthly income exceeding 10000 SR. A total of 384 (80%) were Saudi mothers. As for children's data, most of the mothers had 1-2 children below the age of 14 years where the child was the first for 129 (26.9%) mothers and second for 220 (45.8%). The youngest child was male for 284 (59.2%) and female for 196 (40.8%) mothers (Table 1).

(Table 2). A total of 351 (73.1%) mothers reported that at least one of their children was previously injured which was for 2-3 times among 160 (45.6%) of them, and for more than 3 times among 130 (37%). The most reported causes of injury were accidents (54.2%), fall from height (52%), physical abuse (hitting; 41.7%), injury during playing (34%) and burns (28.7%). The most reported types included bruises and cuts (64.4%), fractures (36.8%), burns (28.7%), and poisoning (17.9%). Regarding site of injury, shoulder / upper extremities was the most frequent site (54.7%), followed by head (54.4%), the back (37%), neck (31.3%), and lower extremities (18.8%).

Table 1. Socio-demographic characteristics of study mothers and their children, Saudi Arabia (n=480)

Socio-demographic data	No	%
Age in years		
< 30	225	46.9%
30-39	161	33.5%
40+	94	19.6%
Residence		
Urban	321	66.9%
Rural	159	33.1%
Residence type		
Private	210	43.8%
Rented	270	56.3%
Residence level		
Ground floor	258	53.8%
High floor	222	46.3%
Social status		
Married	289	60.2%
Separated	159	33.1%
Widow	32	6.7%
Educational level		
Below secondary	64	13.3%
Secondary	226	47.1%
University / above	190	39.6%
Employment		
Housewife	225	46.9%
Governmental sector	124	25.8%
Private sector	99	20.6%
Retired	32	6.7%
Monthly income		
< 5000 SR	192	40.0%
5000-10000 SR	158	32.9%
> 10000 SR	130	27.1%
Nationality		
Saudi	384	80.0%
Non-Saudi	96	20.0%
Children aged less than 14 years		
1-2 children	256	53.3%
3-4 children	224	46.7%
Child order		
First	129	26.9%
Second	220	45.8%
After second	131	27.3%
Child gender		
Male	284	59.2%
Female	196	40.8%

Table 2. Prevalence and pattern of child injury as reported by study mothers, Saudi Arabia (n=480)

Child injury data	No	%
Have any of your children been previously injured?		
Yes	351	73.1%
No	129	26.9%
If the answer is yes, the average number of injuries per month (n=351)		
1 time	61	17.4%
2-3 times	160	45.6%
> 3 times	130	37.0%
The cause of the child injury (n=351)		
Accident	174	54.2%
Fall from height	167	52.0%
Physical abuse	134	41.7%
Injury during playing	109	34.0%
Burn	92	28.7%
The type of child injury (n=351)		
Bruises and cuts	226	64.4%
Fracture	129	36.8%
Others	97	27.6%
Burns	92	28.7%
Poisoning	63	17.9%
Site of injury (n=351)		
Shoulder / upper extremities	192	54.7%
Head	191	54.4%
The back	130	37.0%
Neck	110	31.3%
Lower extremities	66	18.8%
Chest	18	5.1%

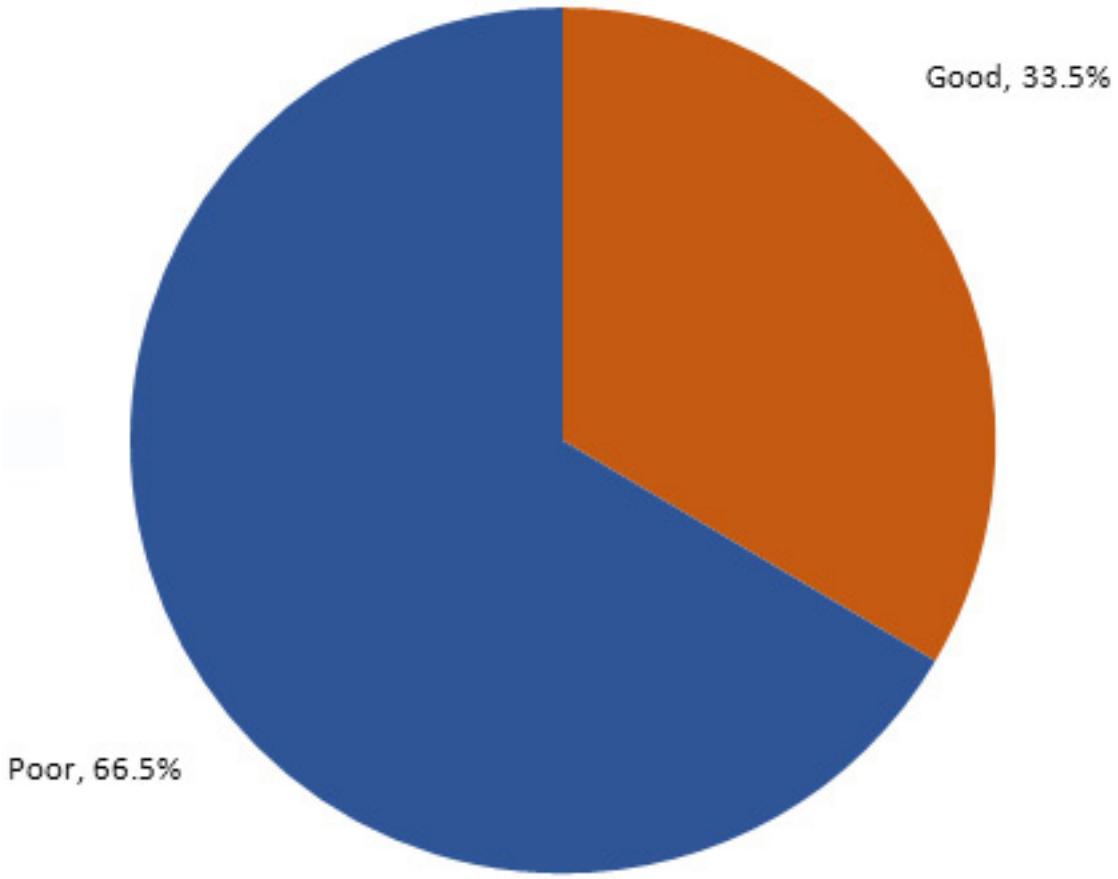
A total of 323 (67.3%) of mothers know about child trauma. As for types, the most known child trauma included fractures (78.8%), burns (59.2%), bruises and cuts (39%), and poisoning (30%). Also, the most known causes of child injuries were playing without safety factors (70.2%), fall (46.5%), physical abuse (28.1%), burns (27.5%), RTA (20%), and poisoning (8.8%). Considering symptoms of childhood injuries, the most known were avoid movement (67.3%), problems with sleeping and eating (54%), aggression (54%), and extreme fear (32.7%). The most reported preventive measures of child trauma by the study mothers included; Prevent children from carrying sharp tools (53.8%), Keep children away from hot and burning materials (49.2%), use designated child seats in the car (45.4%), use baby strollers (45%), and providing safety means at home (42.5%). A total of 220 (45.8%) mothers reportedthat calling emergency is the first action with child trauma, 213 (44.4%) reported going to hospital and 117 (24.4%) said not to move the child but 97 (20.2%) said doing nothing.

Table 3. Maternal awareness and practice of Child Trauma, Saudi Arabia

Awareness items	No	%
Do you know about the child's trauma?		
Yes	323	67.3%
No	157	32.7%
What are the types of injuries in children?		
Fractures	378	78.8%
Burns	284	59.2%
Bruises and cuts	187	39.0%
Poisoning	144	30.0%
Others	98	20.4%
What are the causes of injuries in children?		
Playing without safety factors	337	70.2%
Fall from a height	223	46.5%
Physical abuse	135	28.1%
Burns	132	27.5%
RTA	96	20.0%
Poisoning	42	8.8%
Excessive movement	34	7.1%
Diseases complications	29	6.0%
What are the symptoms of childhood injuries?		
Avoid movement	323	67.3%
Problems with sleeping and eating	259	54.0%
Aggression	259	54.0%
Extreme fear	157	32.7%
Irritability	92	19.2%
Preventive measures of child injuries		
Prevent children from carrying sharp tools	258	53.8%
Keep children away from hot and burning materials	236	49.2%
Use designated child seats in the car	218	45.4%
Use of baby strollers	216	45.0%
Providing safety means at home	204	42.5%
Safety gates	120	25.0%
What is the first practice to deal with children's injuries?		
Calling emergency	220	45.8%
Going to hospital	213	44.4%
Do not move the child	117	24.4%
Nothing	97	20.2%

Overall maternal awareness level about child trauma, Arabia. A total of 161 (33.5%) mothers had an overall good awareness about child trauma while the vast majority (66.5%) had poor awareness level.

Figure 1. Overall maternal awareness level about child trauma, Arabia



Factors associated with mother's awareness about child trauma, Saudi Arabia. A total of 36.2% of old aged mothers had an overall good awareness about child trauma versus 27.6% with a recorded statistical significance (P=.026). Also, 42.7% of those in urban areas had an overall good awareness compared to 15.1% of rural residents (P=.001). Good awareness about child trauma was detected among 54.5% of mother residents in high floors and among 63.7% of highly educated mothers compared to 23.4% of low educated mothers (P=.001). A total of 78.2% of mothers in the governmental sector had high awareness level in comparison to none of retired and 17.8% of unemployed mothers (p=.001). A total of 72.9% of non-Saudi mothers had good awareness, as did 53.9% of mothers with 1-2 children, and 38.7% of those with previously injured child versus 19.4% of those without (P=.001).

Table 4. Factors associated with mother's awareness about child trauma, Saudi Arabia

Factors	Overall knowledge level				p-value
	Poor		Good		
	No	%	No	%	
Age in years					
< 30	163	72.4%	62	27.6%	.026*
30-39	96	59.6%	65	40.4%	
40+	60	63.8%	34	36.2%	
Residence					
Urban	184	57.3%	137	42.7%	.001*
Rural	135	84.9%	24	15.1%	
Residence level					
Ground floor	218	84.5%	40	15.5%	.001*
High floor	101	45.5%	121	54.5%	
Social status					
Married	185	64.0%	104	36.0%	.069^
Separated	102	64.2%	57	35.8%	
Widow	32	100.0%	0	0.0%	
Educational level					
Below secondary	49	76.6%	15	23.4%	.001*
Secondary	201	88.9%	25	11.1%	
University / above	69	36.3%	121	63.7%	
Employment					
Housewife	185	82.2%	40	17.8%	
Governmental sector	27	21.8%	97	78.2%	.001*^
Private sector	75	75.8%	24	24.2%	
Retired	32	100.0%	0	0.0%	
Nationality					
Saudi	293	76.3%	91	23.7%	.001*
Non-Saudi	26	27.1%	70	72.9%	
Children aged less than 14 years					
1-2 children	118	46.1%	138	53.9%	.001*^
3-4 children	201	89.7%	23	10.3%	
Youngest child order					
First	83	64.3%	46	35.7%	.057
Second	138	62.7%	82	37.3%	
After second	98	74.8%	33	25.2%	
Child gender					
Male	188	66.2%	96	33.8%	.884
Female	131	66.8%	65	33.2%	
Have any of your children been previously injured?					
Yes	215	61.3%	136	38.7%	.001*
No	104	80.6%	25	19.4%	

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

Factors associated with child trauma as reported by their mothers, Saudi Arabia. Higher incidence of child trauma was reported among all aged mothers, 81.1% of rural areas, 85.1% of high floor residents, all low educated mothers' children, all non-Saudi mothers' children, 86.8% of mothers with 3-4 children, all older children and 89.4% of male children (P<0.05 for all).

Table 5. Factors associated with child trauma as reported by their mothers, Saudi Arabia

Factors	Have any of your children been previously injured?				p-value
	Yes		No		
	No	%	No	%	
Age in years					
< 30	126	56.0%	99	44.0%	.001*
30-39	131	81.4%	30	18.6%	
40+	94	100.0%	0	0.0%	
Residence					
Urban	222	69.2%	99	30.8%	.005*
Rural	129	81.1%	30	18.9%	
Residence level					
Ground floor	162	62.8%	96	37.2%	.001*
High floor	189	85.1%	33	14.9%	
Social status					
Married	220	76.1%	69	23.9%	.001*
Separated	99	62.3%	60	37.7%	
Widow	32	100.0%	0	0.0%	
Educational level					
Below secondary	64	100.0%	0	0.0%	.001*
Secondary	130	57.5%	96	42.5%	
University / above	157	82.6%	33	17.4%	
Employment					
Housewife	129	57.3%	96	42.7%	
Governmental sector	124	100.0%	0	0.0%	.065^
Private sector	66	66.7%	33	33.3%	
Retired	32	100.0%	0	0.0%	
Nationality					
Saudi	255	66.4%	129	33.6%	.001*^
Non-Saudi	96	100.0%	0	0.0%	
Children aged less than 14 years					.001*
1-2 children	157	61.3%	99	38.7%	
3-4 children	194	86.6%	30	13.4%	
Child order					
First	60	46.5%	69	53.5%	.001*
Second	160	72.7%	60	27.3%	
After second	131	100.0%	0	0.0%	
Child gender					
Male	254	89.4%	30	10.6%	.001*
Female	97	49.5%	99	50.5%	

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

Discussion

The current study aimed to assess maternal knowledge and awareness about child trauma and also to assess frequency rate of child trauma among study participants. Annually, millions of children are sent to hospitals for injuries from accidents that result in permanent disabilities, and thousands of children worldwide pass away as a result of these incidents (19). Accidents affect a person's physical, mental, and social well-being and can result in illnesses, impairments, or even fatalities. Accidents can happen in many different places, but the home is where they happen most frequently when they involve children (20). The preschool years are a crucial time in a child's development, and because of their natural curiosity to explore the environment and their incapacity to understand the risks of their actions that could result in harm or disability, preschoolers are particularly prone to injuries and accidents at home (21).

As for child trauma, the current study revealed that the vast majority of mothers had a child with previous history trauma / injury which was also frequent among most of them. Bruises and cuts, fractures and burns were the most frequent, mainly at upper extremities, head and neck. Accidents, fall, physical abuse and burns were the most reported causes of trauma / injury. Similar findings were reported by Almalki MM et al. (22) in Makkah where about 69% of children experienced trauma, with fall from height the most reported cause and extremities and head were the most affected sites. Another study by Albedewi H et al. (23) found that falls represented 31.9% of child trauma, but 25.1% were due to Motor Vehicle accidents. The main cause of fractures was falls (37.9%), then car accidents (21.5%). Other studies revealed that the child trauma rate was 47.6% (24-33). Children with old aged mothers, those in rural residence, those in residence on higher floors, low education, and mothers with 3-4 children and male children showed significantly higher trauma rate. Many other studies revealed that male children were more liable for trauma (24, 30, 32). Fall from height and MVA with fracture injuries were also the most reported by many studies which are consistent with the current study findings (34-39).

With regard to maternal awareness about child trauma, the current study showed that only one-third of the study mothers were knowledgeable about child trauma irrespective that two-thirds claimed they know about the issue. Higher awareness was about types, causes and symptoms associated with child trauma. Lower awareness was reported for preventive measures and first aid of the trauma. Old age, residence, high education, and having history of child trauma were significantly associated with higher awareness level. Another study by Soltani R and Jahanmehr S (40) revealed that only 28.8% of the mothers had good knowledge about child trauma and its preventive measures which is consistent with the current study findings. In Lebanon, a study showed that more than one-third of the mothers had poor knowledge, while the vast majority showed poor practice level. A much better awareness was reported by Anwar MM (41), Eldosoky RSH (42) where about 83% of the mothers had satisfactory knowledge about child trauma. Another study revealed that about three-quarters of the mothers were knowledgeable about child trauma with a similar high knowledge reported in Nigeria (43) and Saudi Arabia (44).

If early identification and helpful, trauma-informed measures are given, children who have experienced trauma need not have poor physical and mental health outcomes. Early care and education (ECE) settings' caregivers, including parents of small children, should find this especially pertinent. Trauma-informed care can help children in their early years develop resilience and stable attachment relationships with their caregivers, as well as lessen the effects of trauma on brain development and neurophysiology. (18, 45)

Conclusions and Recommendations

In conclusion, the current study revealed that most of the children experienced childhood trauma, mainly contusions and fractures due to falls or accidents which is consistent with the literature findings. Also, the study mothers lack knowledge about child trauma mainly first aid and its preventive measures. Coordinated efforts are needed to create and develop evidence-based educational programs for mothers to help in reducing child trauma rate and associated risks. A national assessment of the burden of childhood injuries, their determinants and risk factors, and the scope of this significant health issue requires more investigation.

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Dementia: Definition, Overview, and Global Epidemiology

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1. Definition and Overview of Dementia

1.1 What is Dementia?

Dementia is a chronic and progressive clinical syndrome caused by various diseases that damage the brain, leading to significant decline in cognitive abilities and loss of functional independence. The term derives from the Latin demens, meaning "out of one's mind," though modern understanding emphasizes its neurological basis rather than purely mental illness.

Dementia affects:

- Cognition → memory, language, reasoning, visuospatial skills
- Functionality → ability to perform everyday activities
- Behaviour and personality → mood, emotions, social interactions

Importantly, dementia is not a part of normal aging. While some cognitive changes are typical with age, dementia involves pathological decline beyond normal expectations for a person's age and education level.

1.2 Subtypes of Dementia

Several distinct disorders can cause dementia, each with unique pathological features:

- **Alzheimer's Disease (AD):**
  - o Accounts for 60–80% of cases
  - o Characterized by amyloid plaques and neurofibrillary tangles
- **Vascular Dementia:**
  - o Results from cerebrovascular disease
  - o Often follows strokes or chronic small-vessel disease
- **Lewy Body Dementia:**
  - o Features fluctuating cognition, visual hallucinations, and Parkinsonian symptoms
- **Frontotemporal Dementia (FTD)**:
  - o Prominent changes in personality, behaviour, or language
  - o Often earlier onset (50s–60s)

Other less common causes include:

- Parkinson's disease dementia
- Huntington's disease
- HIV-associated neurocognitive disorder
- Creutzfeldt-Jakob disease

1.3 Clinical Features

1.3.1 Cognitive Decline

A hallmark of dementia is persistent cognitive impairment. Patients may initially exhibit subtle deficits, progressing to severe disability. Affected domains often include:

- **Memory:** Difficulty recalling recent conversations or events, repeating questions, misplacing items
- **Language (Aphasia):** Word-finding issues, naming errors, reduced comprehension
- **Visuospatial Function:** Difficulty recognizing familiar faces, getting lost, misjudging spatial relationships
- **Executive Function:** Poor planning, difficulty managing finances, impaired decision-making

These changes are often insidious and progressive, with family members noticing subtle shifts before a formal diagnosis.

1.3.2 Functional Impairment

Unlike normal aging, dementia inevitably affects a person's ability to live independently:

Stage	Functional Changes
Early	Misplacing items, forgetting
Moderate	Needs help dressing, cooking,
Severe	Dependent for basic self-care,

Functional decline impacts:
• Instrumental Activities of Daily Living (IADLs): e.g., managing medications, finances
• Basic Activities of Daily Living (ADLs): e.g., bathing, dressing, eating

Functional deterioration is a significant driver of caregiver burden and institutionalization (Lyketsos et al., 2011).

1.3.3 Behavioural and Psychological Symptoms

Over 80% of dementia patients develop Behavioural and Psychological Symptoms of Dementia (BPSD) during the disease (Lyketsos et al., 2011). These may include:

• Depression
• Anxiety
• Apathy
• Hallucinations
• Delusions
• Wandering
• Agitation or aggression
• Sleep disturbances

Symptoms often fluctuate and may worsen in the evening—a phenomenon known as sundowning.
Example: A patient with Alzheimer's might believe their spouse is an imposter (Capgras syndrome) or insist they need to "go home" despite already being at home.

Management includes:
• Environmental modifications
• Non-pharmacologic interventions (e.g. music therapy, structured activities)
• Judicious pharmacologic treatments when necessary

1.4 Dementia vs. Normal Aging

Differentiating dementia from normal aging is essential for early diagnosis. Key differences include:

Feature	Normal Aging	Dementia
Memory Loss	Misplacing keys, later found	Putting keys in the freezer and forgetting why
Recognition	Occasional name lapses	Not recognizing close family members
Language	Slower word retrieval	Profound language deficits
Functionality	Manages daily life independently	Difficulty performing familiar tasks
Orientation	Preserved	Disorientation in time and place

1.5 Dementia Impact on Patients, Families, and Society

Impact on Patients
- Emotional distress, fear, and anxiety
- Loss of independence and social withdrawal
- Progressive cognitive and physical decline

Impact on Families
- Emotional burden and chronic stress
- Financial strain due to medical costs and caregiving
- Physical health risks among caregivers, including higher rates of depression

Societal Impact
- Global costs exceeded USD 1.3 trillion in 2023, projected to double by 2030
- Workforce impact due to caregiver absenteeism
- Healthcare systems under strain, especially in low- and middle-income countries

Effective dementia policy requires public education, caregiver support, early detection, and investment in research (Prince et al., 2015; Alzheimer's Disease International, 2023).

1.6 Historical Perspectives on Dementia

- **Ancient and medieval eras: Dementia viewed as moral failing, supernatural influence, or natural aging.**
- **18th–19th centuries:**
  - o Philippe Pinel differentiated dementia from insanity.
  - o "Dementia" became a medical term for irreversible cognitive decline.
- **1906:**
  - o Alois Alzheimer described plaques and tangles in a woman with progressive memory loss.
  - o Emil Kraepelin named the condition "Alzheimer's disease."
- **20th century:**
  - o Advances in neuropathology showed dementia as a pathological disease, not normal aging.
- **21st century:**
  - o Global health priority.
  - o Focus on modifiable risk factors and early intervention (GBD 2019 Dementia Forecasting Collaborators, 2022).

2. Epidemiology of Dementia

2.1 Global Prevalence

Dementia has emerged as a significant public health concern worldwide. As of 2019, approximately 57.4 million people globally were living with dementia (GBD 2019 Dementia Forecasting Collaborators, 2022). This figure is projected to nearly triple to 152.8 million by 2050 (Brookmeyer et al., 2007; Prince et al., 2013; GBD 2019 Dementia Forecasting Collaborators, 2022).

Age-specific prevalence doubles roughly every five years beyond age 65:

Age Group	Prevalence (%)
65–69	1.5–3
70–74	3–6
75–79	6–12
80–84	12–20
≥85	>30

2.2 Gender Differences

Globally, women account for approximately two-thirds of dementia cases (Prince et al., 2015; GBD 2019 Dementia Forecasting Collaborators, 2022). Factors include:
• Women's longer life expectancy
• Possible biological susceptibility
• Social factors (women more likely to live alone and receive diagnosis)

2.3 Regional Variations

Dementia prevalence varies by region, influenced by:
• Age structure
• Life expectancy
• Genetics
• Environmental and lifestyle factors
• Diagnostic practices

Estimated prevalence in people ≥60 years:

Region	Estimated Prevalence (%)
North America	~6–8%
Western Europe	~7–9%
Eastern Europe	~5–7%
Latin America	~7–9%
Sub-Saharan Africa	~2–4%
Asia-Pacific	~4–6%
Middle East/North Africa	~4–6%

The largest increases in dementia cases between 2019 and 2050 are projected in:
• North Africa and Middle East (+367%)
• Eastern Sub-Saharan Africa (+357%)

By contrast, increases are smaller in:
• High-income Asia Pacific (+53%)
• Western Europe (+74%)

2.4 Drivers of the Dementia Surge

Population Aging & Growth
Most of the rise in dementia prevalence stems from population aging and growth, rather than significant increases in age-specific dementia rates (GBD 2019 Dementia Forecasting Collaborators, 2022).

Modifiable Risk Factors
Key modifiable risk factors include:
• High BMI
• High fasting plasma glucose
• Smoking
• Low education

While these risk factors slightly increase future dementia burden, education gains may offset some risks. Livingston et al. (2020) estimate that addressing modifiable risks could prevent up to 40% of dementia cases.

2.5 Economic and Social Impact

The economic toll is substantial:
• Global dementia costs exceeded USD 1.3 trillion in 2023, projected to double by 2030 (Alzheimer's Disease International, 2023).

Costs include:
• Direct medical expenses
• Social and institutional care
• Informal caregiving burden

Caregiver burden is significant, encompassing:
• Emotional distress
• Physical exhaustion
• Financial strain

Spouses caring for individuals with dementia are at higher risk for depression and anxiety disorders (Prince et al., 2015).

3. Future Outlook and Challenges

• By 2050, low- and middle-income countries are expected to bear 60–70% of the global dementia burden.
• There is an urgent need for:
  o Early detection programs
  o Public education
  o Dementia-friendly policies
  o Investment in prevention, care innovations, and research into disease-modifying therapies

Conclusion

While age-specific dementia rates are largely stable, **the global burden is set to nearly triple by 2050** due to demographic changes. Preparing health systems, societies, and economies for this surge is a critical challenge.

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Are people with obesity to be blamed for their obesity? Uncovering obesity stigma: a Narrative review

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Abstract

Obesity is one of the leading epidemics worldwide. Despite its prevalence, individuals with obesity often face significant weight bias and discrimination across various settings. Bias can manifest in various forms, including teasing, bullying, unfair treatment, disrespect, and misjudgment. It affects people of all ages, regardless of gender, race, or educational background. The consequences of obesity stigma are enormous. It impacts people with obesity at the socioeconomic level, psychologically and physically, which eventually harms their health. In healthcare, obesity stigmatization leads to reduced and delayed access to health services and a lower quality of care. Many strategies and recommendations have been proposed to reduce and hopefully end obesity and weight stigma.

In this review, we discuss definitions, prevalence, biases among healthcare providers, perceptions of bias among people with obesity, the consequences of stigma, and recommended strategies to minimize obesity stigmatization in healthcare.

Keywords: obesity stigma, weight bias, weight discrimination, weight stigma

Introduction

Obesity is one of the leading epidemics worldwide. It is a global public health concern, as it affects both high-income and low-income countries, resulting in a significant economic burden. According to WHO, in 2022, 1 in 8 people are living with obesity worldwide [1]. Moreover, it is estimated that by 2035, 51% of the population aged five and above will be either overweight (BMI ≥ 25 kg/m²) or obese (BMI ≥ 30 kg/m²) worldwide [2]. Obesity is a chronic, relapsing, and multifactorial disease with serious health consequences. It cannot solely be attributed to an individual's diet or lifestyle choices [3,4]. It is defined as abnormal and excessive fat accumulation, which poses a significant health risk [5]. However, despite the high prevalence of obesity in the population, the prevalence of weight discrimination against people with obesity is equally high [3,6]. The World Obesity Federation defines weight stigma as "the discriminatory acts and ideologies targeted towards individuals because of their weight and size" [7]. Weight stigma, also known as obesity stigma, refers to negative social beliefs, attitudes, and behaviors that are directed towards people with obesity. It stems from the belief that people with obesity are at fault for their obesity. In a meta-analysis conducted in 2016, not only was there a high prevalence of weight discrimination; 19.2% of those with class 1 obesity (BMI 30—34.9 kg/m²) and 41% of those with obesity class 2 and above (BMI ≥35 kg/m²); but higher BMI correlates with higher perceived weight stigma [3,8]. In addition, it was shown that women were subject to higher weight discrimination [3,8].

People with obesity face discrimination in their workplace, community, and in healthcare. It affects both men and women, regardless of socioeconomic status, race, or educational level. It also affects people from different obesity categories, from overweight to morbid obesity. There are various forms of bias: teasing, bullying, exclusion, unfair treatment, and shaming. There are common stereotypes and misconceptions about people with obesity, including lack of self-control, laziness, lack of compliance or commitment, poor health/food choices, and lack of hygiene [4]. Despite evidence from research proving that obesity is predominantly due to genetic and environmental factors, obesity continues to be viewed as an individual's wrong choices and decisions about their diet and health [4].

Media is the main culprit behind the stereotypes and the stigmatization; besides, it promotes obesity stigma as a socially acceptable norm [4,9]. In media, whether it is in kids' cartoons, movies, or popular TV shows, obese people are portrayed as ugly, less intelligent, lazy, unsuccessful, and lonely [4]. At the same time, individuals who are underweight or of a healthy weight are often portrayed as successful, smart, socially acceptable, and have friends [9,10]. On the other hand, in a study where people with obesity were positively portrayed, there were fewer weight-based stigmatizing perceptions held by the public —reconfirming the crucial impact of media on obesity stigma [9].

The consequences of this weight stigma are enormous [4]. It affects different domains of life in people with obesity. In relationships, it can lead to feelings of exclusion, teasing, bullying, and name-calling. In education, it can be in the form of lower expectations and achievements. In the work environment, it leads to unequal opportunities, wage discrepancies, and exclusion from co-workers; in healthcare, receiving poor-quality care, incorrect diagnoses, and feeling judged.

Moreover, experiencing weight bias can lead to negative feelings, such as depression, shame, and guilt. It also results in poor self-esteem, body dissatisfaction, stress, and anxiety. This in turn leads to either avoidance behavior, disregard of their health, unhealthy weight loss regimes, or substance abuse. Furthermore, it can lead to increased mortality due to not receiving timely age-appropriate screening tests [11].

Health care providers bias:

Counterintuitively, multiple studies have shown that healthcare providers hold both explicit and implicit negative attitudes toward people with obesity [4,6,11]. In a study among 2,449 adult women on the source of obesity stigma and perceived negative attitudes towards people with obesity, 69% were from doctors, 46% were from nurses, 37% were from dietitians, and 21% were from mental health professionals [12]. Physicians have a strong preference for thin people rather than fat people. Moreover, a strong correlation was found between the physician's own BMI and their bias level. If the physician had a non-obese BMI, their bias towards people with obesity was more substantial, compared to physicians with obese BMI, where their bias was of a moderate level [13]. Additionally, in a study among nurses (N=398), those with lower BMI hold higher negative attitudes towards people with obesity [6].

Furthermore, in a study conducted by Ferrante et al. on family physicians and their attitudes and knowledge of obese patients, it was found that the majority of physicians find dealing with obesity frustrating (66%), while 51% find it useless and ineffective. Moreover, while the majority of physicians were aware of weight loss exercise regimens (60%) and diets (57%), only 19% of physicians knew of community resources for severely obese patients or helpful techniques for examining them (24%) [14].

Multiple studies have shown that obesity stigma leads to less patient-centered care for people with obesity. In a study done among primary care providers (PCP), it was shown that PCP believed that obese patients are less likely to be adherent to treatment or self-care recommendations, are lazy, and are weak-willed. Moreover, they reported having less respect for those who are obese compared to those who are not, which was later reflected in their practice, as obese patients had less time allotted for them in the clinic and less patient education as they perceived this as 'wasted time' [6,11,12]. Another study showed the same healthcare attitudes, where people with obesity have less patient-centered communication, thereby resulting in a 19% higher risk of non-adherence [11].

This is a serious concern as it can result in physicians missing a critical diagnosis since they were likely to attribute grave symptoms to obesity rather than looking beyond obesity as a diagnosis. This, in turn, results in delaying the appropriate referral for further diagnostic tests [11].

Not only can the HCPs, but the healthcare setting can be the source of the stigmatization of people with obesity. Examples of Institutional and structural discrimination include discriminatory policies, a non-inclusive culture, denial of care, or inadequate physical accommodation. Multiple studies have shown that most clinics fail to accommodate individuals with obesity, such as missing extra□large blood pressure cuffs, gowns, appropriate scales, and inadequate chairs in the waiting area, thereby making the healthcare setting environment seem unwelcoming for people with obesity [15].

People with obesity perception of bias:
A study was conducted to examine the public's attitudes towards the weight terminology used by healthcare providers. It demonstrated that the terms: "morbidly obese", "fat", and "obese" were perceived as stigmatizing and blaming and were undesirable, while the terms: 'weight' and 'unhealthy weight' were the most desirable terms by the public. Moreover, the terms 'unhealthy weight' and 'overweight' were perceived as non-judgmental terms that were motivating for the public to lose weight [16].

In a study conducted in Australia, among pregnant women coming for their maternal care, it was found that women with higher BMI were more likely to report a negative maternal care experience during pregnancy and after birth compared with women with lower or normal BMI. This is a significant concern, considering that pregnant and postpartum women are a vulnerable population that is at increased risk of depression [17]. In a trial among obese patients who were candidates for either bariatric surgery or medication for weight loss 43% of 105 bariatric candidates and 21.6% of 214 non-surgery candidates reported disrespectful treatment from healthcare providers due to their weight. Nevertheless, 43% of bariatric surgery candidates and 22.5% of non-surgery candidates reported feeling upset due to comments made by doctors about their weight, and 70% of all candidates felt misunderstood and misjudged [6].

A patient who experiences weight stigma has a high-stress level, which thereby increases the level of cortisol, which is also an obesogenic hormone. This, in turn, makes it harder for them to lose weight and negatively affects their health as it increases their risk of heart disease, stroke, and mental health disorders [11].

In terms of healthcare services, people with obesity feel unwelcome, disrespected, and devalued in the clinical setting. People with obesity frequently report feeling ignored and mistreated in healthcare settings. Moreover, people with higher BMI are three times more likely to say that they have been denied appropriate medical care [18]. Moreover, obese women are less likely to go for routine screening tests for cancer [19]. A study among women (N=216) showed that women with obesity are likely to avoid or delay going to preventative health appointments. Their reasons were weight gain since the last appointments, not wanting to be weighed, having to undress and expose their body, and fear of being told that they need to lose weight [6].

The Consequences and Impact of Obesity stigma on health

The consequences of obesity stigma are enormous. It affects people with obesity psychologically, physically, and socioeconomically [4].

Psychological consequences:
Obesity stigma significantly impacts mental health and results in poor mental health outcomes. Many studies have shown that people with obesity who are exposed to obesity stigma are 32% more likely to develop depression compared to those with normal weight [4].

In a systematic review that looked at mental health associated with weight stigma, it was found that weight bias causes depression, anxiety disorder, and eating disorders [4, 20]. In another study, it was found that obesity stigmatization strongly affects body image dissatisfaction, quality of life, dysfunctional eating, and the severity of depression and anxiety [4]. Studies also show that obesity is associated with social isolation, depression, and an increased likelihood of suicidal thoughts and suicidal attempts [12]. It also has a detrimental effect on self-esteem and body image [20]. A large cross-sectional study (N=22,231) looked at weight discrimination and the prevalence of mental health disorders. It was reported that women were significantly more likely to report weight discrimination compared to men. Moreover, those who perceived weight discrimination were 3.2 times more likely to have perceived stress.

Contrary to common belief, having social support did not buffer the adverse effects of weight discrimination. Additionally, 56% of those who perceived weight discrimination and bias met the criteria of at least one Axis-I disorder, which includes mood disorders, anxiety disorders, eating disorders, psychotic disorders, and dissociative disorders. Furthermore, those who have experienced weight stigma were 2.4 times more likely to have three or more mental health disorder diagnoses compared to those who have not [21].

Health consequences:
In a study of 1,064 participants that examined attitudes towards weight stigma, it demonstrated that 19% of the participants would avoid future medical appointments, while 21% would seek a new doctor if they felt stigmatized by their weight [16].

Another consequence of obesity stigma is poor healthcare services utilization, such as screening programs. Due to previous discrimination experienced in such settings,

obese individuals tend to avoid healthcare facility visits [19]. Multiple studies showed mirroring results where people with obesity are less likely to go for colorectal, cervical, or breast cancer screening [6] in a study that looked at the reasons behind low gynecological cancer screening in white and black African Americans. It was found that obese women were more likely to delay getting routine screening services. Moreover, as the BMI increases, the rate of those women getting routine Pap smears is even lower. In the study, only 68% of women with a BMI of 55 kg/m² had a Pap smear done, compared to 86% of women with lower BMI. The main barriers to getting the screening services were being subjected to disrespectful treatment, embarrassment about getting their weight checked, small medical equipment that was nonfunctional, unsolicited advice about weight loss, and a negative attitude of the doctor. This study has excluded financial reasons since more than 90% of women had health insurance [19]. Similarly, another study done among white women (N=6,419) found that women with severe obesity were significantly less likely to go for cervical cancer screening due to embarrassment and discomfort in a healthcare setting [6]. These are concerning findings, as obesity is a risk factor for cancer, and avoiding age-appropriate screening will increase the incidence of cancer, morbidity, and mortality of people living with obesity.

Counter to public misconception, obesity stigma leads to weight gain rather than weight loss [4, 22]. Chronically pressuring individuals to lose weight triggers an increase in their stress hormone (cortisol); thereby resulting in increased obesity-related mortality. A high cortisol level not only makes weight loss difficult but also worsens glycemic control, increases blood pressure, and causes immune dysfunction [4]. Moreover, individuals who felt stigmatized by their weight were less likely to engage in exercise [23]. This is again demonstrated in a study that examined overweight patients (BMI > 25 kg/m²) who had consulted their primary care physician to discuss weight loss. It was demonstrated that those who felt 'judged' about their weight by their physician were less likely to lose weight, despite the multiple attempts, compared to those who did not [20]. Moreover, more studies are showing medication non-adherence because of obesity stigma [4].

Socioeconomic consequences:
Studies show that obesity stigma leads to wage discrimination. In employment, not only does it lead to wage discrepancies, but it also affects promotion opportunities and career progression and increases the risk of being fired [4,6]. Moreover, in high-income countries, such as in the USA, people with obesity are less likely to be hired, while in Korea, overweight women are paid less than normal-weight women. It also appears to impact educational opportunities [4]. In a survey among overweight and obese women (N=2,249), 25% reported experiencing job discrimination due to their weight [6].

Additionally, they reported that the sources of weight stigma were 54% from co-workers and 43% from supervisors and employers [6]. Regarding education, two studies conducted in Sweden and England have shown that individuals with obesity are less likely to attain higher education [6]. Reasons could be the exposure to bullying in the form of prejudice, rejection, and harassment, thereby making the educational institute a less safe environment for people with obesity [4].

Strategies to End Obesity Stigma in Healthcare

Now that multiple studies have established the existence of weight and obesity stigma in healthcare, we should focus on remediation strategies [24,25]. Besides, healthcare providers are frequently identified as the source of weight bias by people with obesity [26]. While some studies have examined strategies to reduce weight stigma through education and inducing empathy, their evidence on efficacy is lacking, as many have only assessed short-term effects [15]. Therefore, more research and studies are needed to understand which interventions and strategies are effective [24].

Some proposed recommendations for clinicians to reduce bias and stigma are:

1) Assess for any personal weight bias, such as Surveys or Questionnaires with experimental manipulations to identify stereotypes, beliefs, and prejudices [24,26].
2) Provide appropriate education about the complexity of obesity as a disease – it is not only a food problem; genetics, environment, and other factors also play a significant role in obesity. Understand the difference between body size and obesity. It is important to change the narrative on obesity, as it is a complex, chronic, and relapsing disease. Moreover, it is essential to raise awareness about obesity stigma, especially among healthcare providers [15, 25, 26].
3) Appropriate communication: use of a person's first language rather than stigmatizing diagnoses, such as referring to an individual as an "obese patient". Instead, use terms like "patient with obesity". Moreover, obtain patient consent to discuss their weight and inquire about their preference for the language used to refer to it, such as "curvy" instead of "large" and "fat" [15,26,27].
4) Provide a welcoming clinic environment: appropriate waiting areas with comfortable, sturdy furniture. Appropriate size doors and restroom facilities. Appropriate and validated medical equipment such as beds, scales, and blood pressure measuring cuff sizes; privacy when weighing the patients and appropriate gown sizes in the exam rooms [15, 26].
5) Seek staff training, as many negative attitudes towards people with obesity could stem from frustration at treatment failure and lack of progress with the patients [26,28].
6) Screen patient for trauma and bullying and assess their mental health status to provide appropriate support [26].
7) Enlist the help of board-certified obesity medicine specialists [26].
8) Involve policymakers and healthcare stakeholders in reframing the obesity policies and strategies [25].

Conclusion

In conclusion, despite the high prevalence of obesity in the population, the prevalence of obesity and weight bias are equally as high. People with obesity face discrimination in their workplace, community and healthcare settings, too. This discrimination results in detrimental consequences, such as significant negative mental health impact, increased morbidity and mortality due to delay and avoidance of preventive health care and at a socioeconomic level, too. Society should take a firm stand towards reducing obesity stigma as it is not only unethical but worsens and increases obesity. Starting with addressing obesity bias in healthcare is appropriate as HCPs should be more understanding of the chronic and relapsing nature of obesity as a disease.

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Consumer Responses to Rising Egg Prices and Limited Availability in the U.S., with a Focus on California and Nevada: A Systematic Review and Narrative Synthesis

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Abstract

Between 2022 and 2025, egg prices in the United States rose sharply, reaching an average of $5.90 per dozen in early 2025 due to compounded effects from Highly Pathogenic Avian Influenza (HPAI), inflation, regulatory changes, and supply chain constraints. This systematic review synthesizes consumer behavioral responses to egg price volatility and limited availability, focusing on income-level disparities, ethnic and regional differences, and substitution strategies. Following PRISMA guidelines, 41 peer-reviewed studies, market surveys, and government reports (2020–2025) were reviewed, with emphasis on California and Nevada due to their contrasting socioeconomic and regulatory environments. Key findings reveal that lower-income households in both states disproportionately reduced egg consumption or substituted with lower-cost protein alternatives such as legumes, canned fish, or nut butters. In contrast, high-income and urban populations shifted to plant-based commercial egg alternatives. Ethnic minority communities, particularly Black and Hispanic populations, showed greater price sensitivity and were more likely to modify food purchasing habits. Media exposure further shaped consumer sentiment, with reports of panic buying and perceived scarcity. Findings highlight the need for improved public education on affordable, nutritionally equivalent substitutes and equitable food policy interventions to mitigate future disruptions in protein access.

Keywords
Egg inflation, egg shortage, consumer behavior, \protein substitution, California food access, Nevada food insecurity, PRISMA review.

Introduction

In recent years, volatility in the U.S. food system has intensified, placing pressure on household budgets and altering consumption habits nationwide. Among the most visibly affected grocery items has been eggs—a dietary staple valued for affordability, versatility, and nutrient density. From 2022 to early 2025, the price of a dozen eggs nearly doubled, reaching an average of $5.90 by February 2025 [8, 5]. This steep increase was driven by a convergence of factors including ongoing outbreaks of Highly Pathogenic Avian Influenza (HPAI), inflation in agricultural inputs, regional supply constraints, and shifts in regulatory policy such as California's Proposition 12, which mandates cage-free housing for laying hens [6].

Eggs are not only a household staple but also a key nutritional source of protein, choline, and vitamin B12—especially important for vulnerable groups such as low-income families, children, and the elderly [11]. Therefore, disruptions to egg availability, whether through elevated cost or reduced physical supply, carry direct implications for food security and dietary adequacy. These challenges have been especially acute in regions with significant socioeconomic disparity or regulatory complexity.

California and Nevada offer a compelling comparison in this context. California, with its progressive agricultural regulations and diverse urban population, saw more pronounced price shifts linked to cage-free mandates and localized shortages. In contrast, Nevada, with its rural expanses and limited food distribution infrastructure, experienced accessibility issues even when prices remained relatively stable. Both states also reflect ethnic and economic diversity, making them ideal case studies for understanding nuanced consumer responses.

This review systematically examines how American consumers, particularly across income levels and ethnic groups in California and Nevada, responded to egg price spikes and limited availability. It addresses a critical gap in the literature: how market shocks influence food choice behavior and protein substitution, and what this reveals about food resilience in a post-pandemic, inflationary economy.

Methods

This study follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Databases searched include PubMed, Scopus, Google Scholar, USDA Economic Research Service (ERS), Statista, and industry reports (2020–2025). Keywords included: "egg price inflation," "egg shortage USA," "consumer substitution behavior eggs," "California egg prices," "Nevada grocery trends," and "protein alternatives to eggs."

Inclusion criteria: Studies and reports published between January 2020 and June 2025; U.S.-focused data; content on egg price trends, substitution behavior, demographic differences, or regional food access.

Exclusion criteria: Non-U.S. data, production-only reports, opinion pieces.

Graph 1: Increase in average retail egg prices [19]

Data Extraction and Synthesis: This study extracted data on consumer demographics (income, ethnicity, location), price thresholds, food substitution patterns, emotional and behavioral responses, and policy implications. Findings were synthesized thematically and organized into six analytical categories: national trends, income and ethnic disparities, regional behavior (California vs. Nevada), substitution strategies, media influence and policy implications.

Results

Thematic analysis yielded six key domains of consumer response to egg price inflation and supply disruptions: (1) national emotional and purchasing trends; (2) income-based and ethnic disparities; (3) regional differences in California; (4) regional differences in Nevada; (5) protein substitution strategies; and (6) the role of media and perception.

1. National Trends and Emotional Response

National data show that egg price sensitivity has become a visible stressor for many Americans. A 2025 Clarify Capital survey found that 33% of U.S. consumers stopped purchasing eggs unless prices dropped below $5 per dozen, despite a national average of $5.90 [5]. Emotional responses included anxiety, frustration, and disillusionment with grocers and government policy [14]. Widmar and colleagues noted that perceived price gouging became a widespread concern, triggering reactive purchasing [25].

Moreover, egg price increases were felt not only in the home but also in the service industry: restaurants reported increased menu costs and reduced offerings of egg-based dishes [8]. Consumer frustration with fluctuating prices prompted behavior changes even among those not facing food insecurity, indicating broad psychosocial impact.

2. Income-Based and Ethnic Disparities

The burden of egg price inflation was disproportionately experienced by low-income households and ethnic minorities. Several surveys, including those by UserTesting [24] and USDA ERS [22], reported that families earning below $35,000 annually were twice as likely to skip egg purchases or reduce frequency of consumption compared to those earning over $75,000.

Black and Hispanic households, in particular, reported higher levels of food insecurity linked to reduced access to traditionally affordable protein sources. These groups often substituted eggs with lower-cost, shelf-stable proteins such as canned tuna, dried beans, or powdered milk [16,7]. Food banks in major cities such as Los Angeles, Las Vegas, and Fresno noted increased demand for these items during late 2024 and early 2025 [7].

In contrast, high-income consumers were more likely to shift to premium, plant-based substitutes such as JUST Egg, Simply Eggless [18], or mung bean blends [13]. This trend also correlated with increased interest in flexitarian and vegan diets.

3. Regional Consumer Behavior: California

California saw some of the steepest egg price increases nationwide, due to the 2022 enforcement of Proposition 12, which restricted sales of eggs not produced in cage-free environments [9, 2]. Retail prices in urban centers like San Francisco and Los Angeles surged above $6.50/dozen at peak.

Urban and middle-to-high-income Californians responded by adopting:
- Plant-based egg substitutes [12]
- Nutrient-rich vegan recipes that replicate traditional egg-based dishes
- Alternative breakfast staples such as smoothies, oats, or nut butters

Ethnic variations were notable. Asian-American consumers were more comfortable with soy-based alternatives like tofu, which substituted well in both savory and baking contexts [13]. Latinx households were more likely to continue using eggs in traditional cooking, often reducing frequency rather than seeking plant-based replacements.

Food insecurity also rose in low-income California ZIP codes. Public schools in cities like Oakland and Fresno experienced strain in offering breakfast programs reliant on eggs [3]. Emergency food distribution sites adjusted by sourcing powdered egg or shelf-stable proteins.

4. Regional Consumer Behavior: Nevada

In Nevada, rural and semi-rural populations were especially vulnerable—not due to cost alone but to supply disruptions and scarcity. Communities in northern and central Nevada reported persistent shelf gaps in grocery stores, especially during peak avian flu outbreaks in late 2024 [15].

Consumer adaptations in Nevada included:
- Meal rationing—families reduced the number of egg-based meals per week
- Canned protein reliance—notably tuna, sardines, and chicken
- DIY substitutions—flaxseed and applesauce used in baking

Plant-based commercial alternatives were less common in Nevada, both due to limited retail availability and lack of consumer familiarity. Interviews with local extension agents revealed that many consumers were unaware of plant-based egg options or did not trust their nutritional value [20].

5. Substitution Strategies and Nutritional Implications

Consumers across both states employed a range of substitutions for eggs, influenced by availability, culture, and nutrition literacy. Refer to Table 1 below for common alternatives.

Nutritional implications vary. While many substitutions provide protein, some lack choline, B12, or bioavailable iron, nutrients concentrated in eggs. Over time, reduced egg consumption could impact micronutrient adequacy, particularly in young children and older adults [11].

Table 1: Common Egg Substitutes by Demographic Group

Substitute Type	Examples	Demographics Most Likely to Use
Canned proteins	Tuna, sardines, chicken	Rural, low-income households
Plant-based	Tofu, JUST Egg, flax/chia	Urban, higher-income, health-conscious
DIY baking substitutes	Vinegar + baking soda, banana, applesauce	Middle-income households, parents, bakers
Legumes	Lentils, chickpeas	Budget-conscious consumers
Grain-based alternatives	Peanut butter, oatmeal	Children's meals, breakfast-focused households

6. Role of Media and Public Sentiment

Media coverage, particularly during the peak of the avian flu outbreak, amplified perceived scarcity. Widmar and colleagues [25] identified that social media panic-buying posts contributed to stockpiling behavior in major cities. Hashtags like #EggCrisis and #EggFlation trended on platforms such as TikTok and X (formerly Twitter) during Q4 2024, creating feedback loops between perception and actual market strain.

A notable finding is that many consumers misattributed the cause of shortages, blaming retailers or "hoarders," when in fact systemic production disruptions were the root issue [6]. This misperception highlights a need for clear public communication during future food system shocks.

Discussion

This review reveals how a critical food item, eggs, became a case study in consumer adaptability, food insecurity, and nutritional inequality amid economic and public health disruptions. The price surge and supply fluctuations during 2022–2025 were not isolated economic phenomena; they acted as a magnifying lens on broader issues of food system fragility, income inequality, and information asymmetry in consumer markets.

- **Socioeconomic Impact and Behavioral Economics**

Consumer responses closely align with price elasticity theory and behavioral economics: lower-income consumers responded to price shocks with substitution or avoidance, while higher-income consumers were more flexible and exploratory in alternatives [23]. This economic stratification in food adaptability has implications beyond eggs. It suggests that food inflation exacerbates nutritional disparities, particularly when the inflated item is a nutrient-dense staple.

Our findings align with international trends observed during food crises. For example, Rondoni and colleagues [17] observed similar patterns in Europe, where low-income households substituted away from eggs and animal protein in response to price shocks during the COVID-19 pandemic. Yet, the U.S. case is unique in its regulatory fragmentation—state-level policies like California's Proposition 12 intensified supply issues not experienced uniformly across the nation

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- **Nutrition and Public Health Risks**

Eggs offer more than just protein; they are rich in choline, vitamin B12, selenium, and lutein. Substitutes like tofu, legumes, and flaxseed are often nutritionally incomplete, especially for children and seniors [11]. A prolonged reduction in egg consumption could exacerbate micronutrient deficiencies in already vulnerable populations.

School nutrition programs and emergency food providers need guidance on incorporating low-cost, nutrient-dense alternatives that meet these needs. Powdered eggs and fortified cereals may help, but public education on how to build balanced meals without eggs is urgently required.

- **Media, Misinformation, and Crisis Perception**

The review also illustrates how media—especially social media platforms—shape consumer perception. Panic buying, perceived scarcity, and misinformation (e.g., blaming stores or immigrants for shortages) led to behaviors that further strained supply chains. Widmar and colleagues [25] and Morning Consult [14] both documented how emotional decision-making, rather than rational economic behavior, dominated during peak shortage periods.

This suggests a role for public crisis communication strategies. Government agencies and consumer advocacy groups must be proactive in debunking myths, promoting calm, and offering clear guidance on substitutes and nutritional safety.

- **Policy and Programmatic Implications**

Findings point to several policy gaps and opportunities:
• Expand SNAP/WIC coverage to include high-quality protein substitutes, such as plant-based egg alternatives or fortified products.
• Support local egg production through subsidies or infrastructure in rural areas like Nevada.
• Increase public education on affordable, culturally relevant protein options.
• Regulate pricing transparency to mitigate consumer distrust during inflationary periods.

Equity-focused interventions are especially critical. For example, communities with limited grocery access—often food deserts—may need mobile markets or delivery-based subsidy programs to receive stable protein supplies.

Conclusion

Between 2022 and 2025, rising egg prices and fluctuating availability served as a stress test for the U.S. food system—revealing how economic pressure, regulation, and misinformation impact not only what people eat but how they emotionally and behaviorally respond to disruption.

This review finds that consumer responses were shaped by income, ethnicity, geography, and media exposure. Low-income and minority populations disproportionately reduced egg consumption or relied on nutritionally inferior substitutes, while higher-income consumers pivoted to premium or plant-based alternatives. California and Nevada, as case examples, illustrate the regional complexity in response patterns due to legislation, distribution systems, and cultural food practices.

Policy makers, nutritionists, and food system planners must address these disparities with structural interventions and culturally competent education. Ensuring access to affordable, nutritionally complete protein sources during future supply disruptions is not only a matter of food security—but of public health equity.

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Tirzepatide and Cancer Risk

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Abstract

Introduction: Tirzepatide, a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, has revolutionized the management of type 2 diabetes and obesity. Due to its widespread use and chronic nature of treatment, assessing its long-term safety, particularly concerning cancer risk, is crucial. This descriptive review investigates existing research on the association between Tirzepatide use and cancer development.

Methodology: A review of published articles, including a meta-analysis of randomized controlled trials (RCTs), a retrospective analysis of the FDA Adverse Event Reporting System (FAERS) database, and peer-reviewed articles, was conducted, focusing on data from the last five years.

Results: Reviewed RCTs, primarily designed to evaluate efficacy, showed no significant increase in overall cancer events. Cases of pancreatitis were rare and evenly distributed between Tirzepatide and placebo groups in trials like SURMOUNT and SURPASS. Although some studies reported transient, reversible elevations in pancreatic enzymes, long-term follow-up studies specifically designed to assess pancreatic cancer risk are lacking, and the established link between chronic pancreatitis and pancreatic cancer necessitates caution. Regarding thyroid cancer, current evidence from RCTs and meta-analyses, along with FAERS data, does not conclusively link Tirzepatide to an increased risk.

In conclusion, while Tirzepatide demonstrates remarkable efficacy in weight loss and glycemic control, current research, primarily from short-to-medium-term clinical trials not specifically powered for cancer outcomes, shows no firm evidence of an increased cancer risk. Future RCTs with cancer risk as a primary outcome are essential to provide more definitive insights into the long-term safety profile of Tirzepatide.

Key words: Tirzepatide, cancer risk, pancreatic cancer, thyroid cancer

Introduction

Obesity is a pandemic and many anti-obesity medications have been formulated to target it, since it's a chronic condition; patients usually will need to have these medications for a long period of time and potentially be exposed to side effects. Assessing the safety of these medications is very important; the main aim of this descriptive review is focusing on Tirzepatide medication and its risk of cancer.

Tirzepatide is a revolutionized medication with dual-acting glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) receptor activation that has significantly changed the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise. Tirzepatide achieved better glycemic control, body weight reduction in comparison with other anti-diabetic medication with acceptable side effects ,

Tirzepatide has been introduced and marketed as the most effective weight-loss medication of all times. Its sales from the Lilly group; Mounjaro and Zepbound brands were 3.11 billion USA dollars and 1.26 billion dollars respectively for Q3 of 2024 reflecting high demand and use of the medication . Prior to the introduction of these injectable medications, weight-loss surgery was the only effective way to achieve long standing weight loss, yet surgery was invasive and costly. The introduction of this class of medication has proven to be effective and satisfactory for patients.

Patients can get the medication by prescription or over the counter (self-referral/online pharmacies), making it readily available for use and difficult to track down reported side effects. In the Middle East and from my practice most patients get Tirzepatide over the counter and with minimal interaction with a pharmacist. This puts these patients at greater risk of side effects and potentially life-changing effects if they carry risk factors, for example the history of thyroid cancer or pancreatitis.

Tirzepatide shares side effects like those of other well established GLP-1 medications, including gastrointestinal symptoms, nausea, diarrhoea and vomiting, some of which are dose dependent. Other side effects include hypoglycemia, dizziness and abdominal pain to a lesser extent. Various other side effects were mentioned in literature, including pancreatitis risk .

Many studies have looked at various side effects and safety profile of Tirzepatide. Cancer risk was explored in a few research papers and within clinical trials, yet not separately or specifically trialed for that reason. These clinical trials were primarily aimed at proving efficacy and might not have fully unveiled safety issues. The aim of this descriptive review is to investigate research findings linking the use of Tirzepatide and its cancer risk.

Methods

Published articles looking at cancer risk associated with Tirzepatide were reviewed using online search engines; time frame was within the last 5 years and included review of a meta-analysis of randomized controlled trials (RCTs), a retrospective analysis of adverse events that utilized the FDA Adverse Event Reporting System (FAERS) database and some other peer reviewed articles as well as interesting case studies.

Tirzepatide and cancer risk

Theoretical risk of cancer was raised by studies linking use of GLP1 to thyroid and pancreatic cancer.

Tirzepatide (GLP1-GIP) Receptor analogues are contraindicated for use in any patient with personal or family history of thyroid cancer (medullary) as well as patients with multiple endocrine neoplasia type 2 (MEN2). This contraindication was as a result of animal studies . With this fact in mind, most studies and randomized trials excluded such patients.

The association between risk of chronic pancreatitis and pancreatic cancer is well established ; patients with a history of chronic pancreatitis were also excluded from large trials (like SCALE, STEP and SURMOUNT) making it difficult to assess risk of developing pancreatic change/ cancer in this specific population.

The link between obesity and increased risk of cancer is also well known, and patients who underwent weight loss surgery had a reduced incidence of obesity-associated cancers ' , so it could be argued that Tirzepatide as a weight loss agent potentially carries similar benefits and a reduced risk of cancer.

Results

A meta-analysis of randomized controlled trials (RCTs) evaluating the use of Tirzepatide in T2DM, setting a primary safety endpoint to be risk of any type of cancer and secondary end points of specific cancer types - up to April 24, 2024 , was reviewed and some interesting points were evaluated.

9 RCTs enrolling adults with T2DM and with obesity were included. Pediatric population/cancer patients – as well as patients with a family history of cancer were excluded; case studies and observational studies were also excluded from this meta-analysis.

SUPPASS trials were included in this meta-analysis - Seven RCTs have been published - five of which were global and two were regional in Japan.

SUPRASS 1 evaluated 3 doses of Tirzepatide (5-10 and 15mg) as monotherapy against placebo - while SURPASS 2 and 3 compared these 3 doses of Tirzepatide in efficacy and safety to injectable Semaglutide and Insulin Degludec respectively. SUPPASS 5 on the other hand checked the efficacy and safety of Tirzepatide to Insulin Glargine, compared to placebo.

Most of the adverse events were linked to gastrointestinal side-effects but for the purpose of this study we will focus on pancreatitis and cancer risk. SUPRASS trials (1-5) showed symptom free rise in pancreatic enzymes (amylase and lipase), that was reversible on discontinuation . No future studies followed up these patients to assess this risk or sequelae.

SURMOUNT-2 trial, showed three reported cases of pancreatitis, two were taking Tirzepatide 15mg and one on the placebo group. There were no cases of medullary thyroid or pancreatic cancer.

Previous SURMOUNT-1 showed similar results of four cases of pancreatitis, evenly distributed across the treatment and placebo groups. There was no reported medullary thyroid cancer. These results were consistent with previous SURPASS clinical trials.

Discussion

RCTs reviewed were of smaller numbers, and there were no reported cancer events, however researchers documented that their results should be handled with caution due to smaller numbers of trials, smaller numbers of participants and that the primary outcome of these trials were not predefined cancer outcome rather than as serious adverse event. It's very important to consider cancer as a risk and evaluated as a primary outcome in future studies. All studies reviewed considered cancer as a serious adverse event which could affect the true results reviewed.

Tirzepatide and Pancreatic cancer risk

Tirzepatide improves metabolic parameters and weight which positively affects patient's outcome and could have affected the risk of cancer. This statement should be considered with extra caution as studies have shown risk of pancreatitis with other GLP-1 (Exenatide, Liraglutide) and DPP-4 (Sitagliptin, vildagliptin etc.) use, chronic pancreatitis increased risk of pancreatic cancer by 26 fold in comparison with subjects not suffering from chronic pancreatitis, based on data of published studies .

Antidiabetic medications mentioned above are linked to episodes of acute pancreatitis which have a different etiology sequence to chronic pancreatitis, by which the latter have established links to histological changes including infiltration of T-cells and macrophages, fibrotic reaction and reduction in acinar cells, then the hallmark of developing cancer causing pancreatic intraepithelial neoplasia- intraductal papillary mucinous neoplasms and pancreatic duct glands. It takes years for this change to occur - 12 years for normal duct to change to tumor cell - then another 7 years to have metastatic capacity and another 3 years before the disease to be diagnosed and show clinical symptoms .

With these facts in place, any studies that don't cover at least 6 years of observation with any drug have a risk of missing or wrong interpretation on the risks of malignant disease. Such studies are yet to be initiated.

In a cohort historical study conducted in Israel follow up of 3,290,439 person-years of 543,595 adults with diabetes, 1,665 of them developed cancer of pancreas, yet there was no support of increased incidence of cancer over 7 years following starting GLP-1RA treatment to be found; as mentioned above monitoring above 7 years is required for more accurate results.

Subjects with a history of pancreatitis were excluded from large trials (SCALE, SURMOUNT and STEP). That is why it's still not clear what the actual risk of pancreatic cancer is in this population

Tirzepatide and Thyroid cancer risk

Pharmacological studies in rodents linked use of GLP-1RAs to development of medullary thyroid cancer, resulting in a warning on these agents against use in patients at risk. In human beings the expression of GLP-1 receptor in Thyroid C-cells is lower compared to rodents and treatment with Tirzepatide in RCTs has not been found to be associated with significant increase in calcitonin levels. Clinical studies from RCTs and meta-analysis suggest thyroid cancer to be a rare event, but without consistent evidence of increased risk in those receiving GLP-1RA, these studies concluded that there is no conclusive evidence of link between use of GLP1 RA and elevated thyroid cancer risk.

FDA adverse event reporting database published data on use of Tirzepatide and its safety profile in comparison with other GLP-1RA and it showed no increased risk in medullary thyroid cancer or pancreatobiliary side effects. In another study a comparison was made between Tirzepatide and Semaglutide and it showed that Tirzepatide has less association with side effects (pancreatitis, increased HBA1C and thyroid malignancy). When prescribing Tirzepatide, there is no information or guidance for routine thyroid ultrasound or calcitonin check, nonetheless patients with known thyroid nodules should be evaluated.

Tirzepatide and gastrointestinal cancer/ site specific cancer risk

A review of the literature involving a meta-analysis of 90 RCTs showed no significant effect on developing gastrointestinal cancer when GLP-1 was used in comparison with placebo. This was despite preclinical studies that suggested a possible link between GLP-1 use and tumorigenesis . This study was quite strong as the subjects were also followed for an average of just above three years, which is something that wasn't seen in other meta-analysis. Moreover, site specific analysis did not reveal any significant effect in increasing the risk of developing cancer. These studies also didn't confirm the protective effects reported in previous retrospective cohort studies regarding pancreatic, colorectal and hepatocellular cancer.

Conclusion

GLP-1 and in particular Tirzepatide have gained popularity recently due to their role in weight loss, and managing T2DM, Cardiovascular, hepatic and renal disease. Their effectiveness in achieving high weight loss threshold led to a thriving black market and significant concern over off-label use, which also led to shortages. Under these conditions, continuous monitoring and safety profile of these medications is paramount. Regarding the ongoing debate on the research world regarding whether GLP-1 based therapy can increase the risk for specific cancer like pancreatic, thyroid, gastrointestinal and other site-specific cancer, our conclusion from available research showed no firm evidence to favor this hypothesis nor evidence strong enough to rule out such an increased risk.

These clinical trials and research support the current guidelines recommending Tirzepatide for managing obesity and T2DM. This helps in counselling patients and reassuring them about their safety and that there is no association with an increased risk of cancer. Yet continued monitoring, as well as extended follow-up for existing RCTs/ New RCTs, using cancer risk as primary outcome is essential.

There are several outstanding questions regarding Tirzepatide protective mechanisms (anti-cancer pro-oncogenic) effects. Clinical trials addressing these questions will give us a clear idea about its use as anti-diabetic/weight loss as well as its safety in use in cancer patients.

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Atypical Presentation of Celiac Disease in asymptomatic adult with no significant medical history : A rare diagnostic challenge

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Abstract

Background: Celiac disease mainly presents with gastrointestinal symptoms, but atypical presentations, including liver dysfunction, are increasingly recognized.

Case Presentation: We report the case of a 49-year-old asymptomatic healthy gentleman, having mildly elevated cholesterol managed through healthy lifestyle. He had no history of alcohol or drugs intake and a negative family history of Celiac or liver disease. Patient was incidentally found to have markedly elevated liver transaminases on routine blood tests. Subsequent detailed workup for elevated liver transaminases including Celiac serology was normal.

Conclusion: Celiac disease must be considered in the differential diagnosis of the patients with unexplained liver enzyme abnormalities without gastrointestinal symptoms and negative serological tests.

Keywords: Celiac disease (CD), Seronegative Celiac disease (SNCD), Liver enzymes, Gluten-free diet

Introduction

Celiac disease (CD) is an immune-mediated enteropathy precipitated by gluten in genetically susceptible individuals, characterized by villous atrophy and lymphocytic inflammation of the epithelial layer covering the mucosa (1).

Celiac disease (CD) is classically known for gastrointestinal symptoms such as diarrhea, weight loss, and abdominal pain. However in many patients especially adults, extraintestinal manifestations (hepatic abnormalities, dermatological, hematological, skeletal and endocrine) are increasingly recognised (2). These can often be the first or only signs of the disease. Recognizing these can help clinicians diagnose CD earlier and prevent its complications.

Liver involvement in CD, often termed 'Celiac hepatitis', can present as elevation of liver transaminases and can occur without clinical evidence of CD, occasionally leading to significant diagnostic delays (3) if CD is not considered.

Here, we present a rare case of asymptomatic celiac disease diagnosed during investigation of elevated liver transaminases in a person with normal celiac serology.

Case Presentation

A 49-year-old man, physically active and with no significant medical history aside from diet-controlled hypercholesterolemia, underwent routine blood tests revealing:

- ALT: 547 IU/L (normal <50)
- AST: 245 IU/L (normal <45)
- ALP: 145 IU/L (normal <120)

Bilirubin, albumin, clotting profile, viral hepatitis panel (HAV, HBV, HCV, HEV), autoimmune markers (ANA, ASMA, AMA), metabolic workup (iron studies, ceruloplasmin, alpha-1 antitrypsin) were all within normal limits. The Celiac screen serology including TTG IgA and TTG IgG were negative and patient had normal total serum IgA levels (ruling out IgA deficiency which can cause a false negative serological test). HLA typing was not performed. Imaging studies including abdominal ultrasound and MRI of the liver and biliary tree were unremarkable. Ultrasound-guided liver biopsy demonstrated no specific histological features and showed mild portal and lobular inflammation.

In light of persistent liver enzyme elevation an esophagogastroduodenoscopy (OGD) was performed, revealing:

- Normal esophageal and gastric mucosa
- Erythema and erosions in D1
- Scalloping of the folds in D2
- Negative CLO test for H. pylori

Targeted duodenal biopsies with the above findings were obtained and showed villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis, corresponding to Marsh classification 3B, confirming celiac disease (4).

Patient's liver enzymes improved significantly after six months of gluten-free diet, further strengthening the diagnosis of coeliac disease. The patient remained asymptomatic.

Discussion

This case illustrates an atypical presentation of CD manifesting solely as marked liver enzyme abnormalities in a clinically well patient. While mild transaminase elevation is common in CD, severe liver enzyme elevation is rare and may resemble viral or autoimmune hepatitis (3,5).

Seronegative celiac disease (6) though rare, especially in early or patchy disease or in IgA deficiency (7) can occur and necessitates biopsy for definitive diagnosis. Mechanisms proposed for hepatic involvement include immune dysregulation and increased intestinal permeability leading to systemic inflammation.

Celiac disease should be considered in the differential diagnosis of unexplained liver enzyme abnormalities, even in patients without gastrointestinal symptoms or positive serology.

This case illustrates the diagnostic importance of duodenal biopsy in unexplained abnormal liver function tests and the potential reversibility of liver dysfunction with dietary intervention (8).

Conclusion

Isolated liver enzyme abnormalities can be a rare presentation of silent celiac disease. Negative serology does not exclude the diagnosis. Clinicians must maintain a high index of suspicion and consider duodenal biopsy in persistent unexplained liver enzyme abnormalities. Early diagnosis and gluten-free diet initiation can reverse liver dysfunction and prevent further complications.

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Under the blade – or the needle, 'Silicon psychosis'

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Abstract

The pursuit of beauty has long shaped societal standards and personal identities, from ancient times to the modern age. While historical practices like Cleopatra's milk baths or kohl-lined eyes had cultural significance, today's beauty ideals are largely influenced by social media and cosmetic technology. Procedures such as the Brazilian Butt Lift (BBL) have surged in popularity but come with significant health risks, including death, embolism, and infection. Despite warnings from health authorities, many individuals continue to seek risky or unregulated surgeries, often abroad, driven by unrealistic expectations. This piece explores the evolving standards of beauty, the medical concerns surrounding cosmetic interventions, and the social pressures that fuel them.

Key words: aesthetic, cosmetic surgery, social media, body image, health risks.

Introduction and synopsis

Beauty is the obvious new indicator of social worth, and people are always tempted to improve their aesthetic standards. However, the desire for beauty is not a new phenomenon, and well-documented beauty practices have a long history. For instance, Cleopatra, who used a milk bath to keep her beauty alluring, the usage of kohl to darken, define and enhance the eyes, vegetable dyes on cheeks and lips to make them rosy and red, and hair adornments. Also, some went to extremes to conform to the societal identity and the prescribed modes of beauty, like binding of the feet, ritual tattooing, and body scarification.

To draw some points about aesthetics and how they are touching our life especially nowadays we are using the social media platforms, and they have all bombarded a greater impact on the public consciousness with all sorts of cosmetic technology which range from minor to extreme and the kind of things that nowadays people seem to be preoccupied and captivated with like sizable curvy appealing butts for both genders nonetheless. Appearance has become an obsessive focal point for the majority, especially women.

For instance, the trendy Brazilian butt lift (BBL) which has risen concerns, and the recent declaration in the UK according to the advertising standard authority for it posing great risk of death and danger. The Authority stated it is misleading, very imprudent, and proponents are downplaying the seriousness of the health risk associated as is the pressure on targeted customers with their time-bound offers.

The Brazilian butt lifts and the superficial gluteal liposuction, are colourful terms that tempt and allure a lot of people. In 2018, the clinical data showed a high death rate associated with Brazilian butt lifts, and it has been stated that volume augmentation with implants or fat became a trend in 2020.

In 2015 there were reports of intraoperative mortality related problems like pulmonary embolism which has also raised a serious concern, and in 2018 a review stated that injecting in the subcutaneous plane would reduce the mortality rather than being injected in the deeper muscle or crossing the fascia which can be guarded by using intraoperative ultrasound to ensure that the injection has been laid down correctly within the plane only and did not cross the fascia or compromise it causing serious health issues.

So, from that regard it has been stated that injecting in the superficial gluteal seems to be safe as evidence showed that, however despite this, some of the public are still taking risky approaches for the Brazilian butt lifts, by going abroad without considering those raised risks like infection and sepsis and abscess formation that mandate hospital intervention.

Sepsis is a very dangerous and serious condition, especially if it affects the whole body, as it can lead to multiple organ failure. Also, poor techniques can lead to deep venous thrombosis (DVT), pulmonary embolism, fat necrosis, and skin necrosis. On the other hand, liposuction is not as simple as many think and also has a rate of post-operative complications as well as non-surgical procedures like for instance fillers and the celebrity 'Liquid Brazilian Butt Lift' procedure (liquid BBLS). Liquid BBLs involve injecting hyaluronic acid and dermal fillers into the buttocks, and are promoted as risk-free for only a few pounds and able to be performed in as little as 60 minutes.

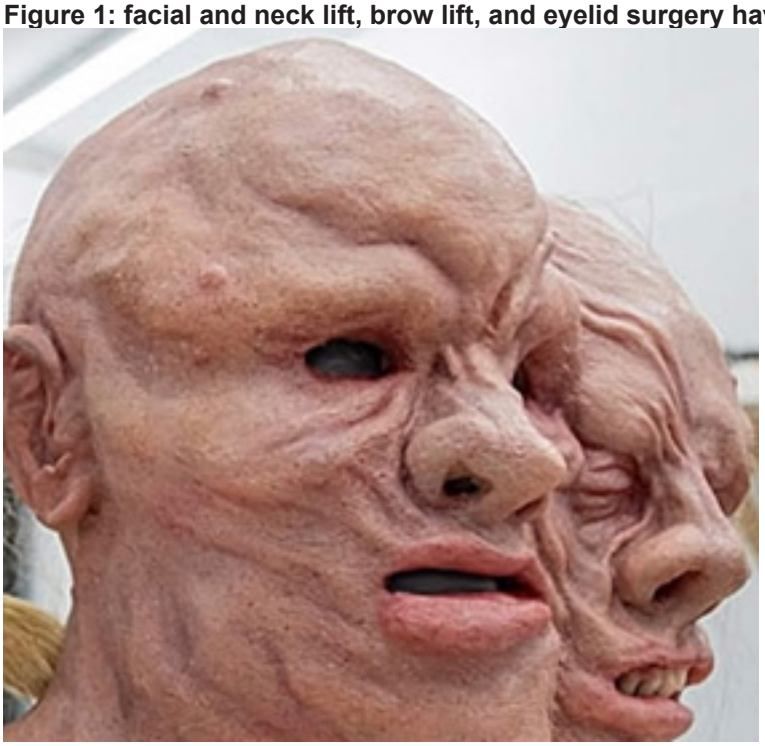
Overall complications include wound disruption, venous thromboembolism, and necrosis and the contour may be uneven and irregular, or there will be leaking of serous fluid leading to seroma, or blood may accumulate under the skin causing haematoma, skin conditions like wound dehiscence, and necrosis and the fatal systemic complication can be embolism whereby the fat travels down to the lung and lodges theree. Other common risks are sepsis and necrotic fasciitis, perforation of intra-abdominal organs.

The incidence of these complaints is not clear, as some are still unreported. However, the reported cases can vary from 2.6 to 20,600 per hundred thousand population and there is no standard technique or analysis to understand the underpinning complications which can be critical, in order, to improve the safety procedures and manage the risks when raised, especially when it comes to the popular procedures given that most are taking place in an ambulatory setting where scarce data are available.

Also, it has been stated that anyone with high body mass index (BMI), as well as liposuction itself, are well-established risks for clotting. This finding isn't new and aligns with previous literature. Also, any prolonged surgical time will be associated with more post-operative complications, including breast augmentation, abdominoplasty, or any other surgery that involves invasion, especially if it involves multiple operations or longer incisions, which would increase the chance of wound dehiscence and other disruptions of the surgical wounds. One study conducted by Pazmino and Garcia showed a high number of deaths were associated with the Brazilian butt lifts which highlights the danger of the procedure (1).

According to the British association of aesthetic plastic surgeons there were 27.465 cosmetic procedures that took place in 2024 with a 5% rise from 2023, and with 94% performed only in women, and the commonest were body contouring including liposuction, abdominoplasty, thigh lifts - which are among the most popular procedures however facial rejuvenations such as facial and neck lift, brow lift, and eyelid surgery have increased and have surged since 2023 (1).

Figure 1: facial and neck lift, brow lift, and eyelid surgery have been surging since 2023.



Risk factors are very important to consider for any procedure with long hours in surgery, like body contouring, liposuction, tummy tucks, and fat grafting which all involve long hours under general anaesthesia, which has its own.

Additionally, in many instances, the outcome can be unexpected , and is often unpleasant to the patient, who walks away unhappy and disappointed.

Also, fat removal from one area and injection into another area can lead to uneven body contour, bumps and lumps, and skin surface irregularities, which, of course, will worsen as the body ages.

All surgeries carry complications which are often downplayed or misunderstood by those requesting these procedures, and they will manifest sooner or later. They can be minor, like infection, scarring, or a life-threatening condition, like organ failure or pulmonary embolism.

The post-COVID time has witnessed a tendency to form clots as COVID in itself is known to increase that propensity with minor symptoms or they can be asymptomatic.

Some patients will wake up after the operation confused, disoriented, or with lingering neurological symptoms.

Certain procedures related to the nose, such as rhinoplasty, where the nose is reshaped, may incur difficulties and those undergoing the procedures often have unrealistic expectations. It carries a low satisfaction rate. The cases where the breasts are enlarged and reshaped can come with a high rate of dissatisfaction, and when it comes to implant themselves, they can rupture, deflate, or harden and contracture, and become asymmetrical (2).

Additionally, a concern has arisen about the association of certain implant types and a rare breast implant-associated anaplastic large lymphoma.

Even if the surgery is ‘successful’, the patient can still walk away unhappy with the outcome. And as we age and the body keeps aging (2). Those procedures might look initially ‘brilliant’, but may quickly become distorted, and the body, as we know, keeps changing with time, with the aging process, and skin loses its elasticity, fat shifts, and there’s nothing that can be done to reverse time.

The troubling thing is that there is no consistent form of regulation, especially nowadays, when many are promoting non-surgical treatment, whether by a trained doctor, or self-taught beautician or ‘beauty influencers’, or cosmetic tourism, which has risen to multiple layers of complexity.

Many nowadays travel abroad for cheaper and promoted types of operations, whereby the package includes offers of accommodation and transportation as part of the deal, and when patients come back home, they will have limited resources and support if something goes wrong under certain conditions.

Also, when it comes to nonsurgical procedures most are promoted as safe. We know the most common types are Botox and fillers, which are in high demand but that doesn’t mean that they are risk-free. The modern hyaluronic acid injection is generally safer than the older version of silicone and can be reversed; however, it can cause granuloma if it becomes infected with certain resistant kinds of bacteria. For the Botox injection it can cause paralysis, nerve damage, or uneven facial results.

Fixation with a youthful beautiful façade has become humdrum in modern society, and has resulted in an upsurge in cosmetic procedures trying to reverse the aging process.

Unrealistic expectations and procedures that cannot turn back time are something we need to think thoroughly about, to save excessive spending and unpleasant disappointments.

Conclusion

In today's world, beauty often equates to social value, pushing many to undergo cosmetic enhancements, sometimes at great risk. Thus, surgery can act as a vehicle for identity and self-expression, and can be empowering for many people, especially those under the spotlight, to gain their confidence in their appearances and their skin; however, to alter the outlook should be subtle and light, and it is vital to approach such surgery with informed caution. The procedure of beautifying can become horrifying or uglifying or disfiguring which is a real and unpredictable outcome in many instances (Figure 1). In some situations, the consequences can be dramatic and permanent, and irreversible.

After all, natural ageing is inevitable, imminent, and no surgery can fully stop its effects or reverse it, although in many instances, we are bombarded with information otherwise. However, subtle, safe choices should be encouraged over drastic changes, with a stronger focus on regulation, education, and realistic expectations. Beauty should enhance, not endanger or disfigure.

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