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ABOUT THE JOURNAL

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The Journal of Medicine and Urban Health (JMUH) is the official journal of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University. JMUH is dedicated to addressing diseases and health issues with the goal of improving the well-being of urban populations. The journal publishes high-quality clinical and basic medical research, health science research—particularly in urban settings—medical innovations, and health policy insights. Publication types include special articles, original articles or systematic review and meta-analysis, review articles, and case reports.

JOURNAL HISTORY

The Journal of Medicine and Urban Health (JMUH)—formerly known as Vajira Medical Journal (established in 1957) and later Vajira Medical Journal: Journal of Urban Medicine (since 2016)—has been in continuous publication for nearly 70 years. The founding editor, Passakorn Kasemsuwan, MD, together with 20 editorial board members, established a strong foundation for the journal. Consistently supported by the Faculty of Medicine Vajira Hospital, Navamindradhiraj University, JMUH has significantly contributed to advancing medical knowledge and practice.

Over the decades, the journal has enhanced the institution's academic reputation by publishing high-quality scholarly works that support both professional recognition and academic career advancement for faculty members, within the institution and across the wider academic community.

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SPECIAL ARTICLE

Epidemiological Status of *Opisthorchis viverrini* Metacercariae in Freshwater Fish Across the Greater Mekong Subregion

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ABSTRACT

Opisthorchis viverrini (a Group 1 biological carcinogen) remains a major public health problem in the Greater Mekong Subregion because of its strong association with cholangiocarcinoma. Given that human infection mainly occurs through the consumption of raw or undercooked cyprinoid fish containing infective metacercariae. This review summarizes the epidemiological status, geographical distribution, host specificity, and transmission dynamics of *O. viverrini* metacercariae in cyprinoid fish across Thailand, Lao People's Democratic Republic (Lao PDR), Cambodia, Myanmar, and Vietnam. The reviewed studies demonstrated considerable geographical variation in *O. viverrini* metacercariae prevalence throughout the Greater Mekong Subregion, with particularly high endemicity reported in Cambodia and Lao PDR, especially within Mekong River-associated ecosystems. In Cambodia, prevalence reached 90.2% in cyprinoid fish from Kandal Province, whereas substantially lower prevalence levels were generally observed in inland regions of Thailand. Species-specific variation was also evident, with *Cyclocheilichthys* spp., *Hampala dispar*, and *Systomus orphoides* identified as important second intermediate hosts in the transmission cycle of *O. viverrini*. Seasonal fluctuations, aquatic ecology, environmental contamination, and inadequate sanitation were consistently associated with transmission intensity. The available evidence indicates that *O. viverrini* metacercariae remain widely distributed in freshwater ecosystems across the region, reflecting the persistent risk of fish-borne transmission in endemic communities. Strengthened surveillance of high-risk cyprinoid fish species, improved sanitation, and sustained behavioral interventions remain essential for reducing transmission and the long-term burden of cholangiocarcinoma in the region.

Keywords: cyprinoid fish, Greater Mekong Subregion, metacercariae, One Health, *Opisthorchis viverrini*

INTRODUCTION

Opisthorchiasis caused by *Opisthorchis viverrini* remains a major food-borne trematode infection in the Greater Mekong Subregion (GMS), particularly in Thailand, Lao People's Democratic Republic (Lao PDR), Cambodia, Myanmar, and Vietnam.¹ Given that *O. viverrini* has been classified as a Group 1 biological carcinogen by the International Agency for Research on Cancer, chronic opisthorchiasis is closely linked to hepatobiliary diseases, especially cholangiocarcinoma (CCA).² The highest endemicity occurs in Northeastern Thailand and Lao PDR, where transmission is strongly associated with the traditional consumption of raw or undercooked freshwater fish dishes, including *koi-pla*, *pla-som*, and *pla-ra*.³

The life cycle of *O. viverrini* involves freshwater *Bithynia* snails as first intermediate hosts and cyprinoid fish as second intermediate hosts carrying infective metacercariae.⁴ Although human infection mainly occurs through the consumption of raw or undercooked cyprinoid fish containing infective metacercariae, viable metacercariae have also been detected in traditional fish products.³ Research has shown marked geographical variation in metacercarial prevalence among cyprinoid fish across the GMS, particularly in Mekong floodplain ecosystems.⁵ High metacercarial prevalence in cyprinoid fish has been reported in Cambodia and Lao PDR, whereas lower but persistent fish-borne endemicity has been observed in several regions of Thailand.^{5,6} Therefore, the surveillance of metacercarial infection in cyprinoid fish remains essential for epidemiological monitoring and disease prevention.⁷ This review summarizes current evidence regarding the prevalence, geographical distribution, host specificity, and transmission dynamics of *O. viverrini* metacercariae in cyprinoid fish throughout the GMS. A summary of the epidemiological studies included in this review is presented in **Table 1**.

CONTENT OF REVIEW

1. Regional Epidemiology of *O. viverrini* Metacercariae

The prevalence of *O. viverrini* metacercariae markedly varies across the GMS, with major endemic hotspots being reported in Thailand, Lao PDR, Cambodia, Myanmar, and Vietnam. Freshwater cyprinoid fish serve as the principal second intermediate hosts sustaining transmission to humans. The prevalence and intensity of infection reported in previous studies are summarized in **Table 2**.

1.1 Thailand

Thailand, particularly the northeastern region, is recognized as a major endemic focus of opisthorchiasis and CCA. According to large-scale surveys across 20 northeastern

provinces, *O. viverrini* metacercariae have been detected in 24.3% of sampling sites, with high infection intensities being reported in the provinces of Amnat Charoen, Nakhon Phanom, Mukdahan, Khon Kaen, and Si Sa Ket.⁸ In Udon Thani Province, the metacercarial prevalence in fish from the Huay Luang Reservoir ranged from 21.6% to 22.8%, whereas surveys in the Nong Han Wetland reported an overall prevalence of 15.1% among 11 cyprinoid fish species.^{4,9} Similarly, surveillance in Nakhon Ratchasima Province demonstrated an overall prevalence of 12.3%; however, some districts showed markedly higher infection rates reaching 78.1%.⁷ In Nakhon Phanom Province, the infection intensity varied geographically, with *Hampala dispar* harboring the highest parasite burden.¹⁰ Transmission is further facilitated through local fish trade networks, where infected fish are widely distributed through regional markets.¹¹

1.2 Lao PDR

Lao PDR remains one of the most highly endemic areas for *O. viverrini* metacercarial infection in the GMS. According to surveys in Vientiane Municipality, the overall fish infection prevalence was 49.5%, with *Cyclocheilichthys apogon* and *C. armatus* showing infection rates of up to 100% in some samples.¹² High prevalence has also been documented in Khammouane Province, particularly within the NamDon, NamPakane, and Mekong River systems, where infection rates reached 51.9% in Thakhek district.⁵ Similarly, studies from Savannakhet and Saravane provinces reported prevalence rates ranging from 38.5% to 42.1%.¹³ Based on these findings, there is widespread and intense transmission in Lao PDR, which is likely associated with the traditional consumption of raw-fish and persistent environmental contamination.^{12,14}

1.3 Cambodia

Cambodia exhibits highly localized transmission of *O. viverrini* metacercariae, particularly along the Mekong River and Tonle Sap Lake systems.⁶ Kandal Province represents a major endemic hotspot, where an exceptionally high prevalence of 90.2% was reported among freshwater fish, with *Systemus orphoides* and *Barbonymus altus* showing infection rates of up to 100%.⁶ In Takeo Province, the metacercarial prevalence reached 38.1%, whereas surveys of market fish in Phnom Penh reported infection rates ranging from 23.7% to 50.0%, indicating widespread distribution through local trade networks.^{6,15} These findings highlight substantial regional variation in endemicity and underscore the importance of freshwater ecosystems, fish trade, and traditional fish consumption practices in sustaining transmission.⁶

Table 1 Summary of Study Characteristics Investigating the Prevalence and Epidemiology of *Opisthorchis viverrini* Metacercariae in the Greater Mekong Subregion

Author	Year	Country	Study Area	Number of Fish Examined	Main Findings
Rim et al.	2008	Lao PDR	Vientiane & Savannakhet	Not specified	High endemicity in Lao PDR, with a 49.5% prevalence in fish from Vientiane Municipality.
Kaewpitoon et al.	2012	Thailand	Nakhon Ratchasima	640 fish	12.3% overall prevalence in fish, with hotspots reaching 78.1% in Sida and KiaKham Thale So districts.
Rim et al.	2013	Lao PDR	3 Provinces	Not specified	Fish infection rate of 14.5% across Luang Prabang, Khammouane, and Saravane.
Prakobwong et al.	2017	Thailand	Udon Thani Province	1,831 fish	Prevalence reached 22.8% near Huay Luang River.
Prakobwong et al.	2017	Thailand	Huay Luang Dam	2,189 fish	Prevalence was 16.9%, intensity in fish peaks during the dry season (January-April).
Phyo Myint et al.	2020	Myanmar	Tachileik (Mekong)	689 fish	Confirmed the first discovery of carcinogenic OvMc in the Mekong region of Myanmar.
Kaensa et al.	2025	Thailand	Nong Han Wetland	392 fish	Average OvMc prevalence in cyprinoid fish was 13.9% across multiple sampling sites.
Prakobwong et al.	2025	Thailand	Udon Thani Province	420 fish	A One Health approach significantly reduced prevalence from 21.91% to 6.0%.
Charoensuk et al.	2026	Thailand	Huay Luang River	1,377 fish	8.5% prevalence; established fishborne trematodes as bioindicators for heavy-metal contamination.

Abbreviation: OvMc, *O. viverrini* metacercariae

Table 2 Prevalence and Intensity of *Opisthorchis viverrini* Metacercariae in Cyprinoid Fish Across the Greater Mekong Subregion

Country	Province/Area	Fish Species	Prevalence (%)	Number of Infected Fish (n)	Number of Examined (n)	Mean Intensity (OvMc/fish)
Thailand	Udon Thani	<i>Henicorhynchus siamensis</i>	27.7%	186	671	17.6
	Udon Thani	<i>Cyclocheilichthys repasson</i>	21.9%	164	748	14.7
	Nakhon Ratchasima	<i>Cyclocheilichthys armatus</i>	19.16%	7	140	ND
	Nakhon Ratchasima	<i>Cyclocheilichthys repasson</i>	18.07%	23	126	ND
	Nong Han Wetland	<i>Cyclocheilichthys apogon</i>	20.3%	37	182	3.7
	Nong Han Wetland	<i>Anematichthys repasson</i>	17.8%	8	45	5.8
	Upper northeast	<i>Mystacoleucus obtusirostris</i>	52.94%	9	17	ND
	Upper northeast	<i>Osteochilus melanopleura</i>	43.47%	10	23	ND

Table 2 Prevalence and Intensity of *Opisthorchis viverrini* Metacercariae in Cyprinoid Fish Across the Greater Mekong Subregion (cont.)

Country	Province/Area	Fish Species	Prevalence (%)	Number of Infected Fish (n)	Number of Examined (n)	Mean Intensity (OvMc/fish)
Lao PDR	Vientiane Municipality	<i>Cyclocheilichthys apogon</i>	100%	15	15	304.1
	Vientiane Municipality	<i>Cyclocheilichthys armatus</i>	100%	20	20	145.1
	Savannakhet	<i>Puntius brevis</i>	92.0%	23	25	360.0
	Savannakhet	<i>Puntioplites falcifer</i>	33.3%	3	9	1.3
	Khammouane	<i>Dangila lineata</i>	69.6%	64	92	2.6 per gram
	Khammouane	<i>Cyclocheilichthys repasson</i>	58.5%	117	195	2.63 per gram
Cambodia	Kandal Province	<i>Systemus orphoides</i>	100%	17	17	37.7
	Kandal Province	<i>Barbonymus altus</i>	100%	14	14	21.6
	Takeo Province	<i>Osteochilus schlegelii</i>	100%	3	3	34.7
	Phnom Penh	<i>Barbonymus schwanefeldi</i>	100%	5	5	74.6
Myanmar	Tachileik (Mekong)	<i>Cyclocheilichthys repasson</i>	2.64%	4	151	2.75
	Yangon City	<i>Puntioplites</i> sp.	10.0%	1	10	1.0
Vietnam	Phu Yen Province	<i>Carassius auratus</i>	28.1%	ND	ND	28.3

Abbreviation: n, number; ND, not determined in the specific study table or text provided; OvMc, *O. viverrini* metacercariae

1.4 Myanmar

In Myanmar, *O. viverrini* metacercariae distribution across several regions remains persistent but at a relatively low endemic level.¹⁶ In Tachileik, which is located within the Mekong River Basin, *O. viverrini* metacercariae were detected in *Cyclocheilichthys repasson* with a prevalence of 2.64% and a mean intensity of 2.75 cysts per infected fish, representing the first documented occurrence of carcinogenic liver fluke metacercariae in this part of Myanmar.¹⁶ Nevertheless, several non-cyprinoid fish species have occasionally been reported to harbor *Opisthorchis*-like metacercariae, although their epidemiological importance remains considerably lower and less clearly defined than that of cyprinoid hosts. In addition, surveys in Yangon City reported *O. viverrini* metacercariae in 2.9% of fish that were examined, including *Anabas testudineus* and *Channa striata*, indicating that low-level transmission may persist within certain urban and peri-urban freshwater ecosystems. However, the contribution of non-cyprinoid fish species to regional transmission dynamics remains uncertain because morphological identification alone may be insufficient to confirm species-level classification of

metacercariae. Consequently, additional molecular and epidemiological investigations are required to clarify the transmission significance of these alternative fish hosts.¹⁷

1.5 Vietnam

In Vietnam, human liver flukes show distinct geographical distribution patterns, with *Clonorchis sinensis* predominating in the northern provinces and *O. viverrini* being mainly endemic in the central and southern regions.¹⁸ This pattern aligns with the broader regional distribution of these parasites within the Lower Mekong Basin. In Central Vietnam, Phu Yen Province has been identified as a critical “hotspot” for opisthorchiasis.¹⁸ Furthermore, according to surveillance of intermediate hosts in this province, crucian carp (*Carassius auratus*) harbor a significant parasite burden, with metacercarial prevalence reaching 28.1% and a mean intensity of 28.3 cysts per fish.¹⁹ In Southern Vietnam, *O. viverrini* metacercariae have been detected in snakehead fish (*Channa striata*) from An Giang Province, albeit at a low prevalence of 1.9%.¹⁸ However, the definitive identification of

O. viverrini in non-cyprinid hosts, including snakeheads, remains challenging. Moreover, early reports often relied on morphological criteria that may overlap with other *Opisthorchis*-like flukes or related species such as *O. lobatus*.^{18,19} Consequently, molecular confirmation and experimental infections are frequently needed to clarify the taxonomic status of these isolates and determine the potential role of non-cyprinoid as viable intermediate hosts.

2. Host Specificity and Transmission Dynamics

O. viverrini transmission involves a broad range of cyprinoid fish hosts reported to harbor infective metacercariae.¹⁸ However, members of the Cyprinidae family are the most epidemiologically important. Several species consistently show high infection burdens, including *Cyclocheilichthys armatus*, *C. apogon*, *Hampala dispar*, *Henicorhynchus siamensis*, *Puntioplites proctozysron*, and *Puntius brevis*, often with high prevalence and intensity.^{7,8,12} In highly endemic areas (e.g., Vientiane Municipality and Savannakhet Province), infection in *C. armatus* and *C. apogon* has reached 100%, with very high cyst burdens per fish.^{12,14} Nevertheless, susceptibility varies markedly among species within the same ecosystem. For example, *Mystacoleucus obtusirostris* has shown high prevalence (52.94%), whereas *Barbonymus gonionotus* exhibits much lower infection rates (1.71%), reflecting species-specific differences in innate susceptibility.²⁰

3. Environmental and Ecological Factors Influencing Transmission

3.1 Seasonal Variation

The transmission dynamics of *O. viverrini* demonstrate marked seasonal variation, with metacercarial prevalence and intensity in cyprinoid fish generally peaking during the dry and cool-dry seasons (November to April).^{4,9} During this period, reduced water levels concentrate snails, fish, and parasites within smaller aquatic habitats, increasing host density and enhancing contact between cercariae and susceptible fish hosts.^{5,9,10} In addition, temperature strongly influences transmission, as warmer conditions (around 34°C) promote *Bithynia* snail infection and cercarial shedding, whereas temperatures exceeding 35°C reduce egg and metacercarial viability.^{9,10} Conversely, the rainy season is associated with increased water volume and flow, which dilute parasite stages and lower infection prevalence in fish despite runoff-associated fecal contamination.⁹ The major environmental, ecological, and behavioral determinants of *O. viverrini* transmission are summarized in **Table 3**.

3.2 Aquatic Ecology and Hydrological Connectivity

Aquatic habitat configuration plays a major role in the transmission dynamics of *O. viverrini*. Lentic environments (e.g., dams and reservoirs) generally exhibit substantially higher metacercarial prevalence than lotic systems, with infection rates reaching 70% in some areas; meanwhile, fast-flowing rivers in Northeastern Thailand showed much lower prevalence rates of approximately 7.7%.⁸ Slow-moving or stagnant waters promote organic matter accumulation and provide favorable ecological conditions for *Bithynia* snails and cyprinoid fish, thereby increasing opportunities for cercarial transmission.⁹ Furthermore, anthropogenic modifications, including irrigation canal construction, may expand transmission hotspots by increasing snail habitats.²¹ By contrast, lotic systems are characterized by stronger water flow that dilutes parasite eggs and cercariae, thereby reducing the transmission efficiency.⁹

3.3 Environmental Contamination

Inadequate waste management is a major driver of sustained *O. viverrini* transmission in freshwater ecosystems. In the Nong Han Wetland of Northeastern Thailand, fecal coliform levels were strongly positively correlated with *O. viverrini* metacercariae prevalence in fish ($r = 0.981$, $P \leq 0.001$), highlighting the role of human waste contamination in creating transmission hotspots.⁹ Open defecation and untreated wastewater discharge introduce large numbers of parasite eggs into aquatic environments, where they are consumed by *Bithynia* snails.^{8,21} Given that natural snail infection rates are typically below 1%, continuous environmental contamination is necessary to sustain transmission and metacercarial infection in fish. Consequently, proximity to contaminated water sources is a significant risk factor for infection in nearby human populations.²²

3.4 Pollution and Heavy Metals

According to recent toxicological research, fish-borne trematode metacercarial infections have been identified as robust, site-specific bioindicators for heavy-metal pollution in freshwater environments. Investigations in Udon Thani Province have determined that cadmium is the strongest predictor of *O. viverrini* metacercariae infection intensity. According to multivariate regression, each 1-ppm increase in cadmium concentration corresponds to an average rise of 5.36 metacercariae/infected fish.²³ Heavy-metal contamination, often derived from community waste (e.g., nickel-cadmium batteries), induces physiological and oxidative stress, which impairs the fish host's immune competence, thereby increasing its vulnerability to parasite establishment.

Table 3 Major environmental, ecological, and behavioral factors associated with *Opisthorchis viverrini* transmission

Factor	Mechanism	Transmission Significance	Supporting Studies
Behavioral: Raw fish consumption	Ingestion of viable metacercariae (OvMc) in traditional dishes such as <i>koi-pla</i> (raw salad), <i>pla-som</i> (short-term fermented), and <i>lab-pla</i> .	Primary driver of human infection; positive correlation between frequency of consumption and infection prevalence.	Prakobwong et al. (2017)
Behavioral: Poor sanitation	Open defecation or the use of unhygienic latrines near water bodies discharges eggs into the environment.	Facilitates the human-to-snail linkage; high fecal coliform levels are strongly correlated ($r = 0.981$) with OvMc prevalence.	Kaewpitoon et al. (2012); Kaensa et al. (2025); Prakobwong et al. (2025)
Ecological: Host feeding behaviors	Certain cyprinids (<i>Hampala dispar</i> , <i>Barbonymus gonionotus</i>) forage in shallow, vegetated shorelines where <i>Bithynia</i> snails and fecal contamination aggregate.	Results in high infection intensity burdens in specific "target" fish species compared to others.	Kaensa et al. (2025); Namsanor et al. (2020)
Ecological: Reservoir host roles	Domestic cats and dogs scavenge on raw fish scraps or discarded rotten fish near reservoirs, shedding eggs into water sources.	Sustains environmental contamination and reinfection cycles even when human cases are treated.	Prakobwong et al. (2017)
Environmental: Seasonality	Receding water levels in the dry season concentrate snails, fish, and parasites, while higher temperatures can boost snail infection rates.	Significant peak in metacercarial prevalence and intensity in fish during the dry season (November–April).	Kaensa et al. (2025)
Environmental: Habitat type	Lentic water bodies (dams/reservoirs) favor organic matter accumulation and slow water flow, conditions that facilitate parasite persistence.	Fish from dams/reservoirs exhibit significantly higher prevalence (up to 70%) than those from lotic river systems (7.7%).	Pinlaor et al. (2013); Prakobwong et al. (2017)
Environmental: Heavy metal pollution	Cadmium concentrations (from community waste like batteries) overlap with high parasite intensity hotspots.	Cadmium was positively associated with higher infection intensity in endemic freshwater ecosystems.	Charoensuk et al. (2026)
Socio-cultural: Gender socialization	In rural communities, consumption of raw fish with alcohol is often associated with traditional "masculine" behavior.	Significant sex disparity; males show 2–4 times greater odds of infection than females across most age groups.	Buathong et al. (2024)
Commercial: Fish trade networks	Improvement in transportation allows parasitized fish to be sold in markets up to 100 km away from their point of capture.	Dispersion of the parasite into non-endemic areas or areas where transmission was previously controlled.	Charoensuk et al. (2022)

Abbreviation: OvMc, *O. viverrini* metacercariae

From a One Health perspective, the co-occurrence of bioaccumulated toxic metals and carcinogenic flukes in commonly consumed fish presents a synergistic public health hazard that may exacerbate the risk of cholangiocarcinoma.²³

4. Sociobehavioral and Economic Drivers

Human infection with *O. viverrini* is primarily associated with the traditional consumption of raw or undercooked

freshwater fish dishes, which may contain viable metacercariae; these parasites are effectively destroyed by prolonged salt fermentation and thorough cooking.³ Domestic animals, especially free-roaming cats, also serve as important reservoir hosts, with reported infection rates ranging from 30% to 53.1%, thereby sustaining environmental contamination and parasite transmission.²⁴ Moreover, higher infection prevalence has been observed among males and individuals aged

40–60 years, likely associated with occupational exposure, traditional dietary practices, and cumulative long-term consumption of infected fish.⁴

5. Public Health Significance and One Health Implications

The current control strategies for opisthorchiasis are increasingly adopting a One Health approach that integrates human, animal, and environmental interventions to interrupt transmission.²⁴ In Thailand, the Lawa Model combines community health education, school-based programs, training of health volunteers, and biological snail control using ducks to reduce *Bithynia* snail populations.²⁵ Similar interventions around the Huay Luang Reservoir in Udon Thani Province significantly reduced human infection prevalence, reservoir host infections, and metacercarial prevalence in cyprinoid fish from 14.1% to 0.9%, 21.3% to 3.8%, and 21.9% to 2.2% over six years, respectively.²⁴ These reductions were largely associated with behavioral changes and decreased consumption of raw fish following targeted health education campaigns.²⁴ Nevertheless, long-term elimination remains challenging because of the persistent cultural practice of consuming raw fish, which leads to frequent reinfection after treatment.²⁴

CONCLUSION

Opisthorchiasis remains a major public health challenge in the GMS because of persistent environmental contamination, high prevalence of infective metacercariae in freshwater fish, and culturally embedded practices of consuming raw fish. Although health education and control programs have successfully reduced infection rates in some endemic communities, sustainable elimination remains difficult because reinfection frequently occurs. Therefore, the long-term control of *O. viverrini* requires continuous surveillance, improved sanitation, behavioral change interventions, and integrated One Health strategies targeting humans, reservoir hosts, and the aquatic environment to effectively reduce transmission and the associated burden of cholangiocarcinoma.

Conflict of Interest

The author declares no conflicts of interest.

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ORIGINAL ARTICLE

A Qualitative Study of the Practice Preferences for Low and Minimal Fresh Gas Flow Anesthesia Using In-Depth Interviews

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ABSTRACT

Objectives: This study primarily aimed to explore the preferences of anesthesia personnel for low (0.5–1.0 L·min⁻¹) and minimal (< 0.5 L·min⁻¹) fresh gas flow (FGF) techniques. The secondary objective was to identify factors influencing their decision-making.

Materials and Methods: After ethics approval, data were collected through in-depth interviews and nonparticipant observation over a 2-month period—from December 2022 to January 2023. This study included four anesthesiologists and six nurse anesthetists.

Results: All participants were females, and 30% were aged 31–40 years. Moreover, 40% had < 5 years of experience in anesthesiology. The duration of clinical practice ranged from 3 months to 28 years (median and mean of 6 years and 10.7 years, respectively). Additionally, 60% were not permanently assigned to a specific anesthesia service. Regarding FGF, 50% used 1.0–1.5 L·min⁻¹, only 30% used 0.5–1.0 L·min⁻¹, and none used < 500 mL·min⁻¹. Five key factors influenced decision-making: personal factors (clinical knowledge and previous hand-on experience), equipment factors (appropriate equipment and monitoring support), patient factors (patient safety concerns and characteristics of the individual patient), institutional factors (practices, policies, and norms of the department), and environmental awareness factor (climate concern).

Conclusion: Low and minimal FGF anesthesia are not yet widely favored by anesthetic personnel in Vajira Hospital. This study shows that the routine use of low and minimal FGF anesthetic technique is influenced by various factors. Although knowledge and hands-on experience are crucial, decisions are also influenced by opinions of coworkers, hospital policies, standard practices, availability of monitoring and equipment, and healthcare financing models such as impact of fix-payment system. All of the abovementioned pose significant barriers to promote the safe and sustainable use of low and minimal FGF techniques.

Keywords: in-depth interviews, low-flow anesthesia, minimal-flow anesthesia, sustainable

INTRODUCTION

The use of low fresh gas flow (FGF) has been proposed as a method for providing general anesthesia since 1995.¹ In 1997, Baxter² presented six categories of flow rates of gases through anesthetic circuits, which remains well-accepted and currently in use: metabolic flow, rate of $< 250 \text{ mL}\cdot\text{min}^{-1}$; minimal flow, rate of $250\text{--}500 \text{ mL}\cdot\text{min}^{-1}$; low flow, rate of $500\text{--}1,000 \text{ mL}\cdot\text{min}^{-1}$; medium flow, rate of $1\text{--}2 \text{ L}\cdot\text{min}^{-1}$; high flow, rate of $2\text{--}4 \text{ L}\cdot\text{min}^{-1}$; and very high flow, rate of $> 4 \text{ L}\cdot\text{min}^{-1}$.

Notably, low and minimal FGF techniques have several advantages. They decrease the amount of inhaled anesthetic agents received by the patient; are cost-effective^{3,4}; help maintain normal body temperature and humidity levels^{5,6}; decrease contamination of anesthetic gases in the operating room^{7,8}; and lower the release of these gases, many of which are greenhouse gases, into the environment.^{9,10} As mentioned above, the remarkable low blood and tissue solubility characteristic of third-generation inhaled anesthetics (e.g., desflurane and sevoflurane) together with the development of modern anesthesia machines and vaporizers promotes the adoption of low and minimal FGF as standard practice.^{11,12}

However, several drawbacks of low and minimal FGF anesthesia may obstruct its wider adoption in clinical practice. Implementing low FGF requires continuous monitoring of both oxygen and anesthetic concentrations. Moreover, flow should be frequently adjusted to ensure patient safety,¹³ and CO_2 absorbents are consumed at a higher rate, increasing the risk of hypercapnia and warranting frequent replacements.^{13,14} Additionally, unwanted or toxic gases such as trace gases (e.g., carbon monoxide, compound A, acetone, and methane) may accumulate in the breathing circuit during low FGF anesthesia.^{14,15}

However, at Faculty of Medicine Vajira Hospital, no study has been conducted on the use of low and minimal FGF in anesthetic services. Therefore, this study aimed to investigate the usage behaviors of anesthetic personnel regarding this technique to assess its popularity and identify factors influencing the decision to use it. This will provide a deeper understanding of how and why anesthetic personnel choose to adopt low and minimal FGF methods and may serve as basis for future research or policy changes.

MATERIALS AND METHODS

This study was qualitative in nature. The sample size was determined based on the case study design, that is, approximately 4–10 cases.¹⁶ The participants consisted

of 10 anesthetic personnel from Vajira Hospital: 4 anesthesiologists and 6 nurse anesthetists who were selected through purposive sampling, with varying years of work experience, age, and anesthetic service unit, and chosen based on the eligibility criterion of having given their consent to participate in the 40-minute observation and 20–40-minute interview.

Data collection was initiated in December 2022, subsequent to ethical approval from the Research Ethics Committee (COA number 170/2565 and subsequent renewal approval to extend the duration beyond the original expiration date). Comprehensive written and verbal information about the study was provided to the anesthesia personnel. For the nonparticipant observation, observers were instructed to maintain a natural and nonintrusive presence to avoid causing discomfort or altering participants' behavior. Observers were not permitted to engage in conversation, provide opinions, and influence participants in any way. The participants retained the right to withdraw from the observation at any point without consequence.

The in-depth interviews were started by an open-ended question by two interviewers who were trained in simulation-based mock interviews, scenario analysis, and rehearsals, emphasizing appropriate language, tone, and demeanor collaborated with the research team to refine their interviewing skills and ensure the credibility, accuracy, and comprehensiveness: "Can you describe your experiences using low flow or minimal FGF anesthesia in your daily clinical practice?" Then, follow-up questions were asked (Table 1). The verbatim transcripts have been analyzed in thematic framework.

Each interview and observation were immediately transcribed verbatim following its completion and was subsequently reviewed multiple times to facilitate a comprehensive understanding of the participants' perspectives. The participants' confidentiality was maintained by omitting their names from the transcribed interview data. To ensure accuracy of the transcriptions, the texts were shared with participants for verification, and their feedback was documented accordingly. An inductive qualitative content analysis (themes emerge from the data) was conducted. The verbatim transcripts were reviewed to generate initial codes, which were then clustered and condensed into overarching themes. Data, through iterative coding and pattern grouping, five main themes were identified. External supervisors with experience in qualitative research were approached for conformability of findings and coding agreement.

Table 1 Semi-Structured Guide of Open-Ended Questions

First Question	Can you describe your experiences using low flow or minimal FGF anesthesia in your daily clinical practice?
Guiding Questions	What led you to decide on that specific flow rate?
	What influenced your decision to use low flow or minimal FGF?
Exploring Questions	Can you describe a <i>recent case</i> when you decided to use low flow or minimal FGF anesthesia? What factors influenced your choice?
	Can you describe a case where your <i>past experience</i> led you to start with low flow or minimal FGF? What about that case made you trust it was appropriate?
	Could you describe a case where <i>patient characteristics</i> influenced your choice of FGF rate? How does the <i>patient's physiology</i> influence your decision between low versus traditional flow?
	How does your <i>department</i> generally view low-flow anesthesia—supportive, neutral, or resistant?
	Can you share your experiences with <i>equipment</i> limitations when attempting low-flow anesthesia?
	How do you <i>monitor inspired and expired oxygen, carbon dioxide and anesthetic agent concentrations</i> during low-flow anesthesia? Can you describe how that informs your decisions?
	Can you describe how concerns about <i>environmental impact</i> like anesthetic gas emissions influence your decisions regarding low flow or minimal FGF?

Abbreviation: FGF, fresh gas flow

RESULTS

At baseline, the characteristics of the study participants are presented in **Table 2** and reflect the initial demographic and clinical features of the enrolled population. The study findings indicate that only approximately 30% of anesthesia personnel at Vajira Hospital routinely employed low FGF anesthesia technique, consistent with findings of previous unpublished surveys among anesthetic personnel at Vajira Hospital that reported usage rates between 25% and 33%. Furthermore, the findings reveal that no personnel routinely utilized minimal FGF anesthesia technique despite the 100% use of third-generation inhalational anesthetics at Vajira Hospital (desflurane and sevoflurane, 51% and 49%, respectively). To identify the determinants of their decision-making process, interview and nonparticipant observation data were analyzed. We conducted thematic analysis: we coded all interview transcripts line by line and identified recurring concepts. Then similar codes were grouped into preliminary themes. Themes raised by participants (informants) as summarize and show in **Table 3**. After that, themes were tested against all transcripts — we looked for whether additional data *reinforced* these themes or introduced *new themes*. After around 7–10 interviews, no new themes emerged; additional interviews simply confirmed existing ones. At this stage, the thematic structure was stable — indicating saturation.

Analysis revealed five primary themes: *personal factors*, *equipment factors*, *patient factors*, *institutional factors*, and *environmental awareness factors*, as show in the **Table 4**.

After grouping the patterns into themes, deriving a hierarchical structure was performed: e.g. How themes relate conceptually. In cases with several emergent themes, which theme is most prominently influential. From the inductive analysis, we found that among these five factors influencing decision-making, certain aspects of decision-making hierarchy were observed. Interestingly, the institutional factor was the most influencing factor, and the environmental concern factor was the least influencing factor. Visualize the structure to hierarchy diagram as shown in **Figure 1**.

DISCUSSION

This study was conducted from December 2022 to January 2023. In some aspects, the information available at that time may differ from current circumstances. The anesthetic machines and monitoring systems may have been replaced with more modern equipment, or the increasing environmental awareness over time may have a greater impact on decision-making. Further research may be required to confirm the results.

The baseline characteristics of the participants, all of whom were females, reflected the reality at the

Table 2 The Baseline Characteristics and Frequency of Fresh Gas Flow Routine Used by Anesthetic Personnel

Category	Number (n)	Percentage (%)
Sex		
Male	0	0
Female	10	100
Professional group		
Physician	4	40
Nurse anesthetist	6	60
Age group		
21-30 years	2	20
31-40 years	3	30
41-50 years	3	30
51-60 years	2	20
Years of experience in anesthesiology		
Less than 5 years	4	40
5-10 years	2	20
11-15 years	1	10
16-20 years	3	30
Anesthesia service unit		
No specific unit	6	60
Cardiovascular surgery	1	10
Pediatric surgery	0	0
Urologic surgery	0	0
Neurosurgery	0	0
Orthopedic surgery	0	0
Others: ENT surgery	1	10
OBG surgery	1	10
Vascular surgery	1	10
Routine FGF rate used		
Less than 0.5 L/min	0	0
0.5 L/min	0	0
0.5–1.0 L/min	3	30
1.0–1.5 L/min	5	50
1.5–2.0 L/min	2	20
More than 2.0 L/min	0	0
Type of inhaled anesthetic used		
Desflurane	N/A	51
Isoflurane	N/A	0
Sevoflurane	N/A	49

Abbreviations: ENT, Otolaryngology; FGF, fresh gas flow; L, liter; min, minute; n, number; N/A, not applicable; OBG, obstetrics and gynecology

Table 3 Summarizes the Themes that Influenced Decision-Making as Attributed to the Informants

ID	Professional Group (experience duration)	Theme				
		Personal	Equipment	Patient	Institutional	Environmental
1	Nurse anesthetist (4 years)	✓	✓	✓	✓	
2	Nurse anesthetist (28 years)	✓	✓	✓	✓	
3	Nurse anesthetist (1 year)		✓		✓	✓
4	Nurse anesthetist (25 years)			✓	✓	✓
5	Nurse anesthetist (20 years)	✓		✓	✓	
6	Nurse anesthetist (7 years)		✓	✓		
7	Anesthesiologist (2 years)	✓			✓	
8	Anesthesiologist (3 months)		✓	✓	✓	✓
9	Anesthesiologist (15 years)	✓		✓		✓
10	Anesthesiologist (5 years)	✓	✓		✓	✓
Number of informants		6	6	7	8	5

Abbreviations: ID, identification

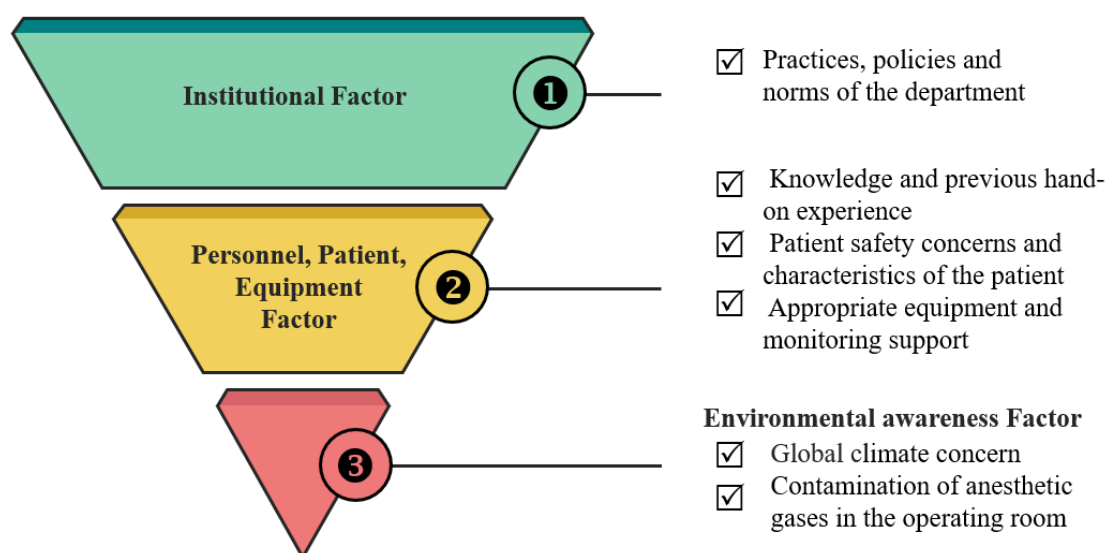
Table 4 Summarizes the Decision-Making Factors for Low-Flow and Minimal-Flow Anesthesia, Supported by Illustrative Quotes from the Interviews

Theme	Description	Illustrative Quotes
1. <i>Personal factors:</i> clinical knowledge and previous hands-on experience	Several participants (6 informants) indicated that limited exposure to low-flow anesthesia during their formal training influenced their reluctance to adopt the technique. Some reported uncertainty regarding the physiological principles and safety parameters associated with low FGF.	"I know the concept, but I was never really trained to use low-flow routinely. I'm afraid I might do something harmful if I reduce the flow too much." - A 28-year experienced nurse anesthetist
2. <i>Equipment factors:</i> appropriate equipment, monitoring support, and availability	The availability of modern anesthesia machines equipped with real-time gas analyzers was determined as a key element. Several participants (6 informants) noted that older machines in certain operating rooms and lacking of gas analyzer did not support accurate monitoring required for low-flow techniques.	"It's not that I'm against low-flow, but it requires more attention. You have to monitor end-tidal gas levels more closely, adjust the vaporizer and change soda-lime more often." - A 7-year experienced nurse anesthetist "We can't use low-flow safely without proper monitoring. In some ORs, we don't even have functioning gas analyzers." - A 3-month experienced anesthesiologist
3. <i>Patient factors:</i> patient safety concerns and characteristics of the individual patient	Concerns about patient safety were revealed, particularly the risk of hypoxia, inadequate anesthetic depth, or hypercapnia or organ-specific damage. Some clinicians (3 informants) preferred to use higher flows for higher-risk patients (e.g., patients with kidney impairment).	"If I'm going with sevoflurane for a patient in stage 3 CKD, I must keep the fresh gas flow comfortably above 1 L/min, because I'm aiming to stay safe, solid, and sure." - A 15-year experienced anesthesiologist "I get a bit uneasy using fresh gas flow below 2 L/min with some anesthetic gases — I'm just worried it might cause problems." - A 4-year experienced nurse anesthetist

Table 4 Summarizes the Decision-Making Factors for Low-Flow and Minimal-Flow Anesthesia, Supported by Illustrative Quotes from the Interviews (cont.)

Theme	Description	Illustrative Quotes
4. <i>Institutional factors:</i> practices, policies, and norms of the department	Peer opinion and departmental culture played a significant role. In settings wherein high-flow anesthesia was the norm, less-experienced staff were hesitant to deviate. Analysis of nonparticipant observation data showed the differences and decision-making hierarchy among less-experienced staff, whether they make decisions autonomously or in environments where they receive input from senior colleagues. Furthermore, many (8 informants) noted a lack of formal institutional economic policy or encouraged low-flow anesthesia practices.	"It really depends on who's leading the case. If they're confident and explain their low-flow approach, it builds our confidence too." - A 25-year-old nurse anesthetist "Even if I use low-flow and save on volatile agents, the hospital still gets the same payment per case. There's no financial motivation to be more efficient." - A 28-year-old anesthesiologist "Speaking of low flow anesthesia, a lot of colleagues feel worry about the risks if gas concentrations aren't stable. Some prefer keeping with higher flows because it feels safer and more predictable, especially in longer or more complicated cases. It's kind of the norm for us—using flow with 1.5-2." - A 5-year experienced anesthesiologist
5. <i>Environmental awareness factors:</i> climate concern and contamination of anesthetic gases in ORs	A minority of participants (5 informants) expressed awareness of the environmental benefits of low-flow anesthesia.	"I know it's good for the environment, but in our department, nobody really brings it up—or takes any action to treat it as a real issue." - A vascular nurse anesthetist "The hospital encourages 'green practices' in the institutional emphasis points, but there's no follow-up or training. There are public media about sustainability in the university, but we don't really get incentive for using low-flow techniques." - A 15-year experienced anesthesiologist "I'm worried about OR air quality, so I support low flow to cut down waste gases. But not everyone is on board yet." - An otolaryngology nurse anesthetist

Abbreviations: CKD, chronic kidney disease; FGF, fresh gas flow; L, liter; min, minute; OR, operating room

**Figure 1** Decision-Hierarchy Triangle among Five Primary Themes

time, as there were no male nurse anesthetists, and only approximately 10% of anesthesiologists were males. The participants were purposely sampled to represent diverse ages and years of work experience. As indicated in the results, 30% of the participants were aged 31–40 years, and 40% had < 5 years of experience in anesthesiology. The duration of clinical practice ranged from 3 months to 28 years (median and mean of 6 years and 10.7 years, respectively). However, the diversity was insufficient to represent each anesthesia service unit. The majority of participants were not assigned to any specific anesthesia service unit. Additionally, the following specialties each had one representative: cardiothoracic, otolaryngology, vascular, and obstetrics-gynecology anesthesia service units. Future studies should focus on each specific service. In pediatric anesthesia, there may be challenges in practicing low-flow and minimal FGF techniques, such as inadequate/imperfect airway sealing, short-term anesthesia with face mask, and slow induction and emergence due to “long time constant” while using lower flow rate.¹⁴

We acknowledge that having a colleague as the interviewer could have influenced participants’ responses due to social desirability bias and relational dynamics within the workplace. The participants might be more likely to give answers that seem socially acceptable or positive rather than their completely honest thoughts—especially on sensitive issues; however, the topics covered in the interviews focus on preferences regarding anesthesia techniques as well as the reasons behind their decision and barriers related. These issues are less likely considered sensitive and are unlikely to affect workplace relationship in the future. Conversely, being familiar with the interviewer, could foster deeper trust and richer contextual insights to the study. To address this, the interviewer maintained neutral prompts, emphasized confidentiality, and reflected on positionality throughout data collection and analysis, consistent with recognized practices for managing interviewer effects in qualitative research.

According to the first question “Can you describe your experiences using low flow or minimal FGF anesthesia in your daily clinical practice?” We do not regard this open-ended question as leading or as priming participants’ responses. Given its open-ended nature, participants are afforded full freedom to express their views without restriction or influence. Subsequently, participants were prompted with guiding questions designed to elicit detailed accounts of recent cases or prior experiences

in which low-flow or minimal FGF anesthesia techniques were employed. As well as the factors that influenced their choice of technique. Factors raised by participants (informants) were further examined through probing questions, allowing us to explore the underlying considerations shaping their choices.

Regarding the number of participants, data saturation was achieved when no new themes relevant to the research question emerged. A sample of 10 participants was sufficient to provide the depth needed to identify key themes; this may be because of the homogeneity of the data. Traditional qualitative research practices often utilize fixed numerical thresholds, commonly indicating sample sizes ranging from 5 to 30 participants per group.¹⁷ In contrast, current evidence-based recommendations emphasize a flexible, context-specific approach to sample size determination, based on data saturation.¹⁸

The study findings indicate that only approximately 30% of anesthesia personnel at Vajira Hospital routinely employed low FGF anesthesia techniques. These findings are comparable to those of a survey conducted in North London in September 2016, which found that only 36% of cases had a flow rate of < 1 L·min⁻¹.⁴ A global survey conducted from April 2021 to April 2022 reported that 41% of personnel do not use low-flow anesthesia (defined as <1 L·min⁻¹), and only 15% use minimal-flow techniques. However, since this is a global survey, it cannot be evaluated based solely on numerical data. Each country differs in terms of specific details and context, as noted in the same study. “*There is a correlation between higher income countries and implementation of more sustainability strategies, probably due to better access to updated technology and sustainability education programs*”.¹⁰

Analysis of interview and nonparticipant observation data revealed the decision hierarchy among the five primary themes: the institutional factor was at the most influencing factor, and environmental awareness factor was the least influencing factor (Figure 1).

For the implication, based on our study results, hospital policies should support the standardized use of low and minimal FGF anesthesia where clinically appropriate. For example, outline criteria for when to use low or minimal FGF: clear guidance reduces variability and helps clinicians feel confident applying evidence-based techniques. Integrate low and minimal FGF anesthesia into quality improvement and audit cycles, Include in the hospital policy a requirement to

regularly organize workshops, simulation sessions, and peer-sharing forums for less experienced personnel to enhance competency and confidence in relevant clinical practices, include low and minimal FGF in procurement and equipment standard: including the accurate oxygen and anesthetic gas analyzers, the circuit systems designed to minimize leaks and support rebreathing safely, the software or interface tools to assist clinicians in titrating flows. These hardware standards ensure that clinicians have the tools needed to implement low-flow and minimal FGF anesthesia effectively and safely—helping policy translate into practice. Implementation of such policies can harmonize patient safety, institutional sustainability and cost-efficiency goals. Interestingly, the interview findings indicated the need for concrete or measurable outcomes as motivation for adopting low-flow and minimal FGF anesthesia practices; for example, in a low-flow anesthesia promotion project at the Royal Free Hospital, the goals were to decrease the number of volatile agent bottles ordered per month by 20%⁴ and to decrease the volatile cost per month or the yearly carbon footprint,¹⁹ among others. Demonstrating such quantitative outcomes in clinical practice could influence decision-making and promote the use of low-flow techniques. In practice, anesthesia costs in Vajira Hospital are typically charged on a flat hourly rate. Therefore, even if anesthesia personnel reduce the use of volatile agents, the hospital's revenue remains unchanged, making the cost savings less immediately visible or impactful.

The present study is one of the first attempts to assess the practice preferences for low and minimal FGF among anesthetic personnel at Vajira Hospital and identify factors influencing the decision through in-depth interviews. This study focused not only on “what”, but also on “how” and “why.” This study had a few limitations. Participants were recruited by purposive sampling, with varying years of work experience, age, and anesthetic service unit. However, the diversity of anesthesia machines used was not considered. The sample may not be representative of anesthetic personnel who work with automated low-flow anesthesia systems, such as the AISYS® system (GE, Madison, Wisconsin), wherein the anesthesiologist sets a target alveolar concentration (FA_t) of the volatile agent and a target end-expired oxygen concentration (FaO_2). Once targets are set, the system automatically adjusts FGF and agent delivery to reach and maintain those targets efficiently without constant manual intervention.

CONCLUSION

Top-down and bottom-up policies are crucial to promote low-flow and minimal FGF anesthesia. Top-down strategies include institutional guidelines, mandatory monitoring equipment, financial incentives, and integration into routine practice. In contrast, bottom-up approaches involve empowering anesthesia providers through peer learning and environmental awareness campaigns and fostering a supportive departmental culture. Regular feedback, open conversation, and reassuring safety concerns are beneficial for reinforcing practice change. Together, these approaches enable the safe and sustainable adoption of low-flow techniques across all levels of the healthcare system. Quality improvement research is critical to clearly demonstrate the tangible benefits of using low-flow and minimal FGF anesthesia as routine practice in the hospital.

Conflict of Interest

There are no conflicts of interest.

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Author Contributions

Conceptualization: T.T.
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 Formal analysis: T.T., K.L.
 Funding acquisition: T.T.
 Investigation: T.T., K.L.
 Methodology: T.T.
 Project administration: T.T., K.L.
 Resources: T.T.
 Software: T.T.
 Supervision: T.T.
 Validation: -
 Visualization: T.T.
 Writing – original draft preparation: T.T.
 Writing – review & editing: T.T., K.L.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author, Tanawadee Teeratchanan. The data are not publicly available due to their containing information that could compromise the privacy of participants.

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ORIGINAL ARTICLE

Association between Frailty and All-Cause In-hospital Mortality in Elderly Patients in Internal Medicine Wards, Vajira Hospital

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ABSTRACT

Objectives: Geriatric syndromes such as frailty are becoming more significant in healthcare. Frailty is characterized by increased vulnerability to stressors and decreased physiological reserve in elderly people. Studies in the community and hospice care settings have shown relationships between frailty and morbidity, hospitalization, and mortality. This study aimed to investigate the association between frailty and short-term outcomes in hospitalized Thai older adults.

Materials and Methods: This prospective cohort study included 140 inpatient department patients aged ≥ 60 . The patients or their close relatives were interviewed and assessed for frailty using the Thai version of the FRAIL scale within the first 48 hours of admission, and the patients were followed up at 2 and 4 months for in-hospital mortality. The evaluated secondary outcomes comprised 30-day readmission, length of stay, and hospital costs per day. Results were expressed using risk ratios and mean differences, with $p < 0.05$ indicating statistical significance.

Results: Among the 140 patients examined, 77 (55%) were determined to be frail according to the Thai FRAIL scale, and 63 (45%) were non-frail. In-hospital mortality rates were higher in the frail group than in the non-frail group 13 (16.9%) vs. 3 (4.8%). Multivariate analysis revealed that frail patients were 3.32 times more likely to die during admission than non-frail patients (adjusted risk ratios: 3.32; 95% confidence intervals: 1.12–9.86; $p = 0.031$).

Conclusion: Frailty was associated with higher short-term mortality among older adults admitted to a Thai hospital. Larger, multicenter studies are needed to confirm these findings.

Keywords: frailty, hospital costs, in-hospital mortality, length of stay, readmission

INTRODUCTION

Thailand is facing a demographic transition, with individuals aged ≥ 60 years comprising 20.4% of the total population as of 2022.¹ As this proportion continues to increase, the healthcare system is increasingly challenged by age-related syndromes. One such condition is frailty, which is characterized by decreased physiological reserve and increased vulnerability to stressors,² placing older adults at greater risk for adverse outcomes.

Frailty prevalence in 2005–2021 was 5%–15% among the elderly population in Thailand.³ As the aging population grew, the clinical significance of frailty in predicting health outcomes in hospitalized patients has gained considerable attention. Studies in the community and hospice care settings have shown relationships between frailty and morbidity, hospitalization, and mortality^{4–8}; however, only a few studies were conducted in hospital settings.

Hao et al. evaluated the association between frailty and in-hospital mortality and readmission in elderly patients who received medical care in acute geriatric wards in West China Hospital, Sichuan University, using Frailty Index to diagnose frailty. After 3-year follow-up, it was concluded that frail older adults had higher mortality and readmission rates than robust older adults.² Frailty was significantly associated with increased mortality and poorer functional outcomes in stroke patients.⁹ Some additional evidence of frailty significantly associated with infectious diseases.¹⁰ However, data from Thailand remain limited despite the country's growing elderly population.

Existing studies confirm that the FRAIL scale has high sensitivity and specificity compared with the phenotype criteria. The FRAIL scale to assess frailty status, a scale based on self-report that does not require activities affected by the disease itself.¹¹ This study aimed to investigate the association between frailty assessed using the validated Thai version of the FRAIL scale and in-hospital mortality from all causes in elderly patients admitted to Internal Medicine wards for disease treatment in Vajira Hospital, Bangkok, Thailand.

MATERIALS AND METHODS

This study was a prospective cohort study conducted in Vajira Hospital, Bangkok, Thailand. It included patients aged ≥ 60 years who were admitted to the general Internal Medicine wards for treatment of illnesses between September 25, 2023, and November 10, 2024, and were able to provide formal consent. Patients admitted for appointed procedures were excluded. In cases of inability to consent (i.e., during intubation,

under sedation, or with decreased awareness), the patient's closest relative was asked for consent and interviewed. If both the patient and their representative were not available or did not consent, the patient was not included in the study.

This study utilized the Thai FRAIL scale to screen for frailty, which was validated for reliable and accurate identification of frailty in elderly patients in the Thai context.¹² Five domains (i.e., fatigue, resistance, ambulation, illnesses, and loss of weight) were assessed using five simple questions—one question for each domain. Each question had two predefined answers, rated as 0 or 1, depending on the presence of characteristics related to frailty in each domain. Scores ranged from 0 to 5, and the cutoff for frailty was 3 or above. This tool was used instead of the full Frailty Index questionnaire, as it was simpler and well-suited for elderly patients in our context.

On the day of inclusion (referred to as "Visit 1"), patients were interviewed, and their medical records were evaluated for baseline characteristics: age, sex, weight, height, marital status, cause of admission, severity of disease, comorbidities (especially those included in the Thai FRAIL scale and Charlson Comorbidity Index), medications in use, and diagnoses in current admission. Then, they were assessed for ability to perform activities of daily living (ADLs) using the Barthel ADL Index and nutritional status according to nutrition triage (NT) nutritional assessment form and were screened for frailty with the Thai FRAIL scale. The Barthel ADL Index classified patients into three groups: group 1, independent; group 2, partially dependent and able to do some ADLs; and group 3, unable to perform ADLs and totally dependent. NT nutritional assessment form categorized patients into four groups by severity of malnutrition, namely, no malnutrition or at risk of malnutrition (NT-1), mild malnutrition (NT-2), moderate malnutrition (NT-3), and severe malnutrition (NT-4). Patients were determined to be frail if their scores on the Thai FRAIL scale were ≥ 3 .

Two months after Visit 1 (referred to as "Visit 2"), we obtained each patient's discharge status, length of stay, total hospital cost, and consecutive admissions within 30 days after discharge from the admission wherein they were included. If the patient had not yet been discharged, they would be followed for those outcomes again at 4 months after Visit 1 (referred to as "Visit 3").

A sample size of 280 patients (140 patients in each group) was calculated using results from a study by Hao et al.,² based on prospective study design with

consideration of 5% dropout rate. This study found mortality rates among elderly patients with and without frailty of 28.6% ($p_1 = 0.286$) and 14.5% ($p_2 = 0.145$), respectively. The sample size ratio for the comparison group to the study group was set at 1.5, based on population proportion.¹³ However, this preliminary analysis includes the first 140 patients enrolled, with follow-up and analysis completed.

Categorical data were expressed as percentages and continuous data as means and standard deviations or medians and interquartile ranges. The frail and non-frail patients were compared using Chi-square test or Fisher's exact test for categorical data and independent samples t-test or the Mann-Whitney U test for continuous data. The association between frailty and outcomes were analyzed using multiple regression analysis. Results were described using risk ratios (RR) and 95% confidence

intervals (CI) for all-cause in-hospital mortality and 30-day readmission and mean/median differences and 95% CI for length of hospital stay and hospital cost per day.

Statistical analyses were performed using the IBM SPSS Statistic software for Windows, Version 28.0 (IBM Corporation, Armonk, NY, USA) and Stata Version 13.0 (StataCorp, College Station, TX, USA), with $p = 0.05$ indicating statistical significance. This study obtained ethical approval (COA 162/2566) from the Institutional Review Board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University.

RESULTS

In total, 155 older adult patients were admitted to designated wards. Among the 140 patients included (Figure 1), 77 (55%) were determined to be frail according to the Thai FRAIL scale, and 63 (45%) were

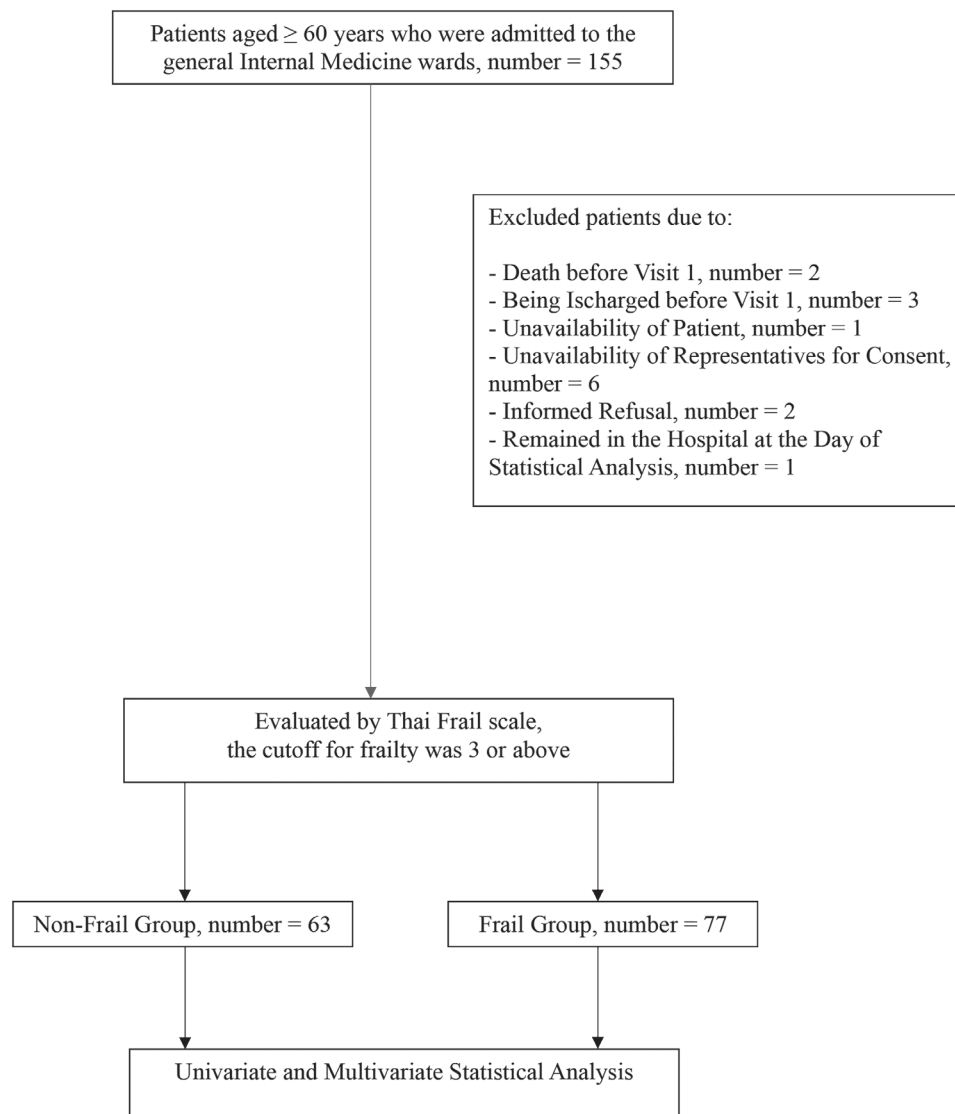


Figure 1 Flow Diagram of the Study

non-frail. Fourteen were excluded for reasons of death before Visit 1 (two patients) or being discharged before Visit 1 (three patients), unavailability of patient at Visit 1 (one patient, undergoing hemodialysis at the time), unavailability of representatives for consent (six patients), and informed refusal (two patients). One patient remained in the hospital at the day of statistical analysis and thus was not included.

Table 1 shows the baseline characteristics of the frail and non-frail groups. Moreover, 67.9% of the included population were below 80 years old, and the average age was 75.45 years. The most common cause of admission was infection related disease (58.6%). The most common underlying illnesses included hypertension (77.1%), diabetes (49.3%), chronic kidney disease (52.9%), and ischemic stroke (22.9%). Polypharmacy was reported in 85.7% of the patients, and 66.4% had high comorbidity burden (Charlson Comorbidity Index ≥ 5). Most patients (62.1%) were able to perform basic ADLs (Barthel ADL Index group 1). Furthermore, 43.6% of the patients were malnourished (NT-2 to NT-4).

Significant differences were noted in sex, comorbidity burden, functional status, and nutritional status between the frail and non-frail groups. There were 2 times more females than males in the frail group. Larger percentages of patients in the frail group were found to have more comorbidities (according to the Charlson Comorbidity Index), be dependent on caregiver (according to the Barthel ADL Index), and suffer from malnutrition than in the non-frail group. Other characteristics were not significantly different between the two groups (**Table 1**).

Compared with non-frail elderly patients, frail patients were more likely to die during admission from any cause (16.9% vs. 4.8%, $p = 0.031$) (**Table 2**). Univariate analysis on the primary outcome demonstrated that frail elderly patients had a higher risk of death from any cause during admission (unadjusted RR: 3.55; 95% CI: 1.05–11.95; $p = 0.041$). After adjustment for age, sex, body mass index (BMI), marital status, cause of admission, severity of disease, Charlson Comorbidity Index, nutritional status, polypharmacy, and the presence of anticholinergics, benzodiazepines, and pain control, it was found that frail patients were 3.32 times more likely to die during admission than non-frail patients (adjusted RR: 3.32; 95% CI: 1.12–9.86; $p = 0.031$) (**Table 2**). **Figure 2** shows the survival analysis based on primary objective outcome among non-frail group and frail group.

For secondary outcomes, no significant differences were found in 30-day readmission rate, length of stay, and hospital cost per day (**Table 2**). The 30-day readmission rates were 19.5% and 9.5% for the frail and non-frail groups, respectively. The median lengths of stay for both groups were 6 days. The median hospital costs per day were 4865.38 Thai Baht (THB) for the frail group and 4853.16 THB for the non-frail group.

DISCUSSION

This prospective cohort study demonstrated an association between frailty, as defined by the Thai FRAIL scale, and all-cause in-hospital mortality among elderly patients admitted to Internal Medicine wards. Frail patients were more likely to die during hospitalization compared to non-frail patients. Although no significant differences were observed in secondary outcomes such as 30-day readmission, length of stay, and hospital costs per day, the mortality association underscores the critical prognostic value of frailty screening upon admission.

Our findings are consistent with previous Thai studies utilizing the FRAIL scale. A prospective cohort study performed by Suraarunsumrit et al. (2025) at Siriraj Hospital. This retrospective cohort study included medical inpatients aged ≥ 60 years old. They were classified into robust, prefrail, and frail groups using the FRAIL scale. Infection was the most common reason for admission in this study. Frailty was significantly associated with higher in-hospital mortality and healthcare utilization, validating the use of the FRAIL scale in academic medical settings in Thailand.¹⁴ However, a previous study demonstrated that frail patients had significantly higher odds ratio of in-hospital acute infections and adverse events compared to non-frail patients. Various frailty tools and definitions were used, with the frailty index being the most frequently employed tool.¹⁵ In a cross-sectional study in Thailand, reported similar findings among elderly patients with medical conditions. Most of the patients had multiple risk factors for frailty such as chronic disease and polypharmacy. Using the Thai Frailty Index, they found that frail patients the risk of hospitalization, more complications, and elderly patients with frailty (both physical and cognitive frailty) had poorer quality of life.¹⁶ These studies underscore the significance of the FRAIL scale as a practical, low-resource screening tool in Thai acute care settings.

In contrast to Western studies,^{4,11,15} wherein frailty assessments are often incorporated into routine geriatric care, several Thai hospitals still lack standardized frailty

Table 1 Demographic and Clinical Characteristics of Elderly Patients in Internal Medicine Wards According to Frailty Status (n = 140)

Variables	Total (n = 140)	Non-Frail (n = 63)	Frail (n = 77)	P-value
All patients	140 (100.0)	63 (45.0)	77 (55.0)	
Age (years)	75.45 ± 9.29	73.98 ± 9.03	76.65 ± 9.39	0.091 ^a
< 80	95 (67.9)	45 (71.4)	50 (64.9)	0.413 ^b
≥ 80	45 (32.1)	18 (28.6)	27 (35.1)	
Sex				
Male	64 (45.7)	38 (60.3)	26 (33.8)	0.002 ^b
Female	76 (54.3)	25 (39.7)	51 (66.2)	
Body Mass Index (kg/m ²)	23.03 ± 4.70	23.78 ± 5.02	22.43 ± 4.35	0.091 ^a
Underweight (< 18.5)	22 (15.7)	9 (14.3)	13 (16.9)	0.567 ^b
Normal (18.5-22.9)	53 (37.9)	22 (34.9)	31 (40.3)	
Overweight (23.0-24.9)	23 (16.4)	9 (14.3)	14 (18.2)	
Obesity (25.0-29.9)	30 (21.4)	16 (25.4)	14 (18.2)	
Morbid Obesity (≥ 30)	12 (8.6)	7 (11.1)	5 (6.5)	
Marital Status				
Single	30 (21.4)	16 (25.4)	14 (18.2)	0.102 ^c
Married	62 (44.3)	32 (50.8)	30 (39.0)	
Widowed	41 (29.3)	12 (19.0)	29 (37.7)	
Divorced/Living Separately	7 (5.0)	3 (4.8)	4 (5.2)	
Cause of Admission				
Infectious Cause	82 (58.6)	38 (60.3)	44 (57.1)	0.113 ^b
Myocardial Infarction	8 (5.7)	5 (7.9)	3 (3.9)	0.082 ^c
Heart Failure	12 (8.6)	6 (9.5)	7 (9.1)	0.515 ^b
Stroke	8 (5.7)	4 (6.3)	4 (5.2)	0.438 ^c
GI Hemorrhage	9 (6.4)	5 (7.9)	4 (5.2)	0.132 ^c
Acute Kidney Injury	6 (4.3)	3 (4.8)	3 (3.9)	0.268 ^c
Electrolyte Imbalance	7 (5.0)	3 (4.8)	4 (5.2)	0.416 ^c
Other	8 (5.7)	3 (4.8)	5 (6.5)	0.548 ^c
Severity of Disease at Admission				
Infection with Septic Shock	12 (8.6)	5 (7.9)	7 (9.1)	0.102 ^c
Shock Condition on Admission (exclude septic shock)	2 (1.4)	0 (0.0)	2 (2.6)	NA

Table 1 Demographic and Clinical Characteristics of Elderly Patients in Internal Medicine Wards According to Frailty Status (n = 140) (cont.)

Variables	Total (n = 140)	Non-Frail (n = 63)	Frail (n = 77)	P-value
Underlying Disease				
Hypertension	108 (77.1)	48 (76.2)	60 (77.9)	0.808 ^b
Diabetes Mellitus	69 (49.3)	33 (52.4)	36 (46.8)	0.508 ^b
Liver Disease	12 (8.6)	7 (11.1)	5 (6.5)	0.332 ^b
Chronic Kidney Disease	74 (52.9)	28 (44.4)	46 (59.7)	0.071 ^b
KDIGO Staging				0.005 ^b
G1	23 (16.4)	8 (12.7)	15 (19.5)	
G2	44 (31.4)	28 (44.4)	16 (20.8)	
G3a	14 (10.0)	6 (9.5)	8 (10.4)	
G3b	15 (10.7)	1 (1.6)	14 (18.2)	
G4	23 (16.4)	13 (20.6)	10 (13.0)	
G5	9 (6.4)	3 (4.8)	6 (7.8)	
ESRD on RRT	12 (8.6)	4 (6.3)	8 (10.4)	
COPD	11 (7.9)	4 (6.3)	7 (9.1)	0.754 ^c
Asthma	3 (2.1)	2 (3.2)	1 (1.3)	0.588 ^c
Angina	8 (5.7)	3 (4.8)	5 (6.5)	0.730 ^c
Heart Failure	28 (20.0)	11 (17.5)	17 (22.1)	0.497 ^b
CAD/MI	29 (20.7)	8 (12.7)	21 (27.3)	0.034 ^b
PAD	2 (1.4)	1 (1.6)	1 (1.3)	1.000 ^c
Old CVA/TIA	32 (22.9)	8 (12.7)	24 (31.2)	0.010 ^b
Hemiplegia	14 (10.0)	2 (3.2)	12 (15.6)	0.015 ^b
Dementia	14 (10.0)	3 (4.8)	11 (14.3)	0.062 ^b
Arthritis	24 (17.1)	9 (14.3)	15 (19.5)	0.417 ^b
CTD	3 (2.1)	0 (0.0)	3 (3.9)	0.252 ^c
Peptic Ulcer	3 (2.1)	1 (1.6)	2 (2.6)	1.000 ^c
Solid Tumor	17 (12.1)	5 (7.9)	12 (15.6)	0.168 ^b
Local	9 (6.4)	3 (4.8)	6 (7.8)	0.428 ^c
Metastatic	8 (5.7)	2 (3.2)	6 (7.8)	
Leukemia	1 (0.7)	1 (1.6)	0 (0.0)	0.450 ^c
Lymphoma	0 (0.0)	0 (0.0)	0 (0.0)	NA
AIDS	2 (1.4)	0 (0.0)	2 (2.6)	0.501

Table 1 Demographic and Clinical Characteristics of Elderly Patients in Internal Medicine Wards According to Frailty Status (n = 140) (cont.)

Variables	Total (n = 140)	Non-Frail (n = 63)	Frail (n = 77)	P-value
Charlson Comorbidity Index	5.74 ± 2.13	5.11 ± 1.87	6.25 ± 2.21	0.001 ^a
< 5	47 (33.6)	28 (44.4)	19 (24.7)	0.014 ^b
≥ 5	93 (66.4)	35 (55.6)	58 (75.3)	
Medication				
Polypharmacy	120 (85.7)	50 (79.4)	70 (90.9)	0.052 ^b
Anticholinergics	41 (29.3)	13 (20.6)	28 (36.4)	0.042 ^b
Benzodiazepines	37 (26.4)	13 (20.6)	24 (31.2)	0.160 ^b
Pain Control (NSAIDs, opioids)	37 (26.4)	15 (23.8)	22 (28.6)	0.525 ^b
Barthel ADL Index				
Group 1	87 (62.1)	55 (87.3)	32 (41.6)	< 0.001 ^b
Group 2	18 (12.9)	3 (4.8)	15 (19.5)	
Group 3	35 (25.0)	5 (7.9)	30 (39.0)	
Nutritional Status				
NT-1	79 (56.4)	48 (76.2)	31 (40.3)	< 0.001 ^c
NT-2	33 (23.6)	9 (14.3)	24 (31.2)	
NT-3	23 (16.4)	6 (9.5)	17 (22.1)	
NT-4	5 (3.6)	0 (0.0)	5 (6.5)	
FRAIL Scale	2.48 ± 1.24	1.33 ± 0.78	3.42 ± 0.57	< 0.001 ^a

Abbreviations: ADL, activity of daily living; AIDS, acquired immunodeficiency syndrome; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CTD, connective tissue disease; CVA, cerebrovascular accident; ESRD, end-stage renal disease; GI, gastro-intestinal; KDIGO, kidney disease improving global outcomes; kg, kilogram; m², square meter; MI, myocardial infarction; n, number; NA, data not applicable; NSAIDs, non-steroidal anti-inflammatory drugs; NT, nutrition triage; PAD, peripheral arterial disease; RRT, renal replacement therapy; TIA, transient ischemic attack

Data are presented as number (%), mean ± standard deviation or median (interquartile range).

P-value corresponds to ^aIndependent samples t-test, ^bChi-square test or ^cFisher's exact test.

Table 2 Univariable and Multivariable Analysis for Comparison of Outcomes of Elderly Patients in Internal Medicine Wards According to Frailty Status (n = 140)

Outcomes	Non-Frail (n = 63)		Frail (n = 77)	Univariable Analysis		Multivariable Analysis		
				Adjusted RR/MD (95%CI)	P-value	Adjusted RR/MD (95%CI)	P-value	
In-Hospital Mortality	3	(4.8)	13	(16.9)	3.55 (1.05-11.95) ^a	0.041	3.32 (1.12-9.86) ^b	0.031
30-Day Readmission	6	(9.5)	15	(19.5)	2.05 (0.84-4.98) ^a	0.115	1.71 (0.74-3.48) ^b	0.356
Length of Stay (days)	6	(4-9)	6	(4-12)	3.98 (-0.11, 8.08) ^c	0.057	4.66 (-0.09, 8.62) ^d	0.084
Total Hospital Cost	35086.75 (23406.5-70658)		32029.5 (17783.75-51805.25)		22964.05 (-1851.79, 47779.89) ^c	0.070	20986.86 (-3215.46, 44751.78) ^d	0.102
Hospital Cost per Day	4853.16 (3896.81-7083.13)		4865.38 (3463.92-6691.75)		449.35 (-2583.36, 3482.06) ^c	0.772	-735.46 (-3112.32, 1329.68) ^d	0.534

Abbreviations: CI, confidence interval; MD, mean difference; n, number; NA, data not applicable; RR, risk ratio

^a Unadjusted risk ratio estimated by Poisson regression with robust standard errors.^b Adjusted risk ratio estimated by Poisson regression with robust standard errors adjusting for age, sex, body mass index, marital status, cause of admission, severity of disease, underlying disease, Charlson Comorbidity Index, polypharmacy, anticholinergics, benzodiazepines and pain control.^c Unadjusted mean difference estimated by Generalized linear model with Gaussian family, with robust standard errors.^d Adjusted mean difference estimated by Generalized linear model with Gaussian family, with robust standard errors adjusting for age, sex, body mass index, marital status, cause of admission, severity of disease, underlying disease, Charlson Comorbidity Index, polypharmacy, anticholinergics, benzodiazepines and pain control

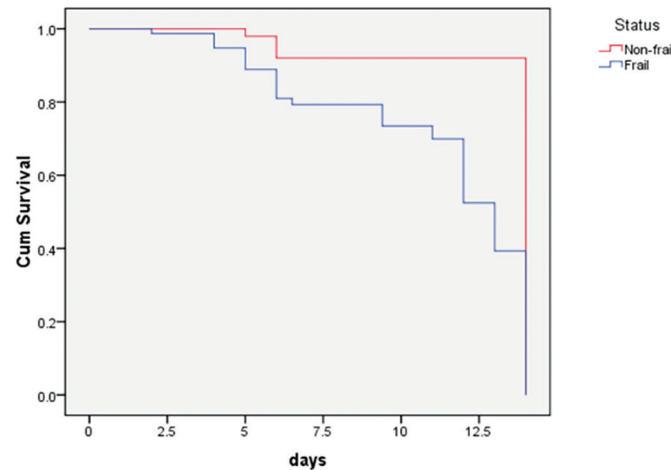


Figure 2 Survival Analysis Based on In-Hospital Mortality among Non-Frail Group and Frail Group

screening protocols. Our findings indicate the need for systematic frailty assessment in acute medical admissions in Thailand, given its rapidly aging population and limited specialized geriatric services. The FRAIL scale is a practical, culturally adapted, and time-efficient tool that can be administered by general staff without requiring extensive training.

Although the present study showed a significant difference in in-hospital mortality, no significant differences were observed in 30-day readmission rates and healthcare costs. These discrepancies may reflect differences in discharge planning, access to post-acute care, or social support systems and warrant further investigation. Moreover, this study did not find a significant difference in length of stay, in contrast to previous reports.¹⁴ A discharge planning system may reduce the length of hospital stays for patients with acute diseases. In addition, this may also be due to the differing characteristics of patients.

This study had several limitations. First, this is a preliminary analysis with a sample size smaller than originally planned, which may limit the potential to detect significant differences in secondary outcomes. Inclusion of more patients could increase accuracy of the study. Second, although some covariates were adjusted, residual confounding—particularly from delirium and functional trajectory—might have influenced outcomes. Third, the FRAIL scale remains a subjective measure and may be affected by recall bias or cognitive impairment in the respondent. Fourth, patients who died before frailty assessment were excluded. This cause leading to underestimation of frailty prevalence and biased

mortality comparisons. Last, as the study was conducted in a single urban tertiary care center, generalizability to other settings, including rural hospitals or community health centers, may be limited. The variation of patient case mix, discharge practices, and resource availability at Our hospital may not reflect other Thai hospitals or international settings.

This study contributes to the association of the FRAIL scale and in-hospital short-term mortality among elderly inpatients. Frailty screening in elderly inpatients may enhance risk stratification, guide clinical decision-making, and prompt early multidisciplinary interventions for inpatients. Future research should investigate whether targeted interventions based on frailty status—such as early mobilization, medication review, vaccination program and nutritional support—can improve clinical outcomes and reduce avoidable mortality in frail older adults.

CONCLUSION

Frailty was associated with higher short-term mortality among older adults admitted to a Thai hospital. The routine frailty screening may help risk stratification and clinical decision-making in acute in-patient settings. Larger, multicenter studies are needed to confirm these findings.

Conflict of Interest

The authors declare that they have no competing interests related to this study.

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Author Contributions

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Formal analysis: C.S., C.P.

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Investigation: -

Methodology: C.S., C.P.

Project administration: -

Resources: -

Software: -

Supervision: C.P.

Validation: -

Visualization: -

Writing – original draft preparation: C.S., C.P.

Writing – review & editing: C.P.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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ORIGINAL ARTICLE

Highly Effective Postpartum Contraceptive Use among Urban Thai Women with and without Gestational Diabetes Mellitus: A Comparative Cross-Sectional Study

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ABSTRACT

Objectives: Gestational diabetes mellitus (GDM) is associated with increased risks in subsequent pregnancies, making effective postpartum contraception essential. This study compared the use of highly effective contraceptive methods at 6 weeks postpartum in urban Thai women with and without GDM. The use of other contraceptive methods in both groups was also examined.

Materials and Methods: This comparative cross-sectional study was conducted at a tertiary care hospital in Bangkok, Thailand. Postpartum women attending routine 6-week follow-up visits between February 5, 2021, and July 7, 2021, were enrolled. Women with recent GDM were compared with women without GDM. The primary outcome was the proportion of women using highly effective contraception (female or male sterilization, or long-acting reversible contraception) at 6 weeks postpartum. Secondary outcomes included the use of non-highly effective contraceptive methods. Multivariable logistic regression evaluated associations between GDM status and contraceptive choice while adjusting for potential confounders.

Results: A total of 156 women were included (78 with GDM and 78 without GDM). The use of highly effective contraceptive methods did not differ significantly between the GDM and non-GDM groups (44.9% vs. 32.1%, $p = 0.100$). However, female sterilization was more frequently selected by women with GDM than by women without GDM (39.8% vs. 18%, $p = 0.003$). The use of non-highly effective contraceptive methods tended to be lower in the GDM group, although the difference did not reach statistical significance (39.8% vs. 55.1%, $p = 0.054$). After adjustment, GDM was independently associated with female sterilization selection (adjusted odds ratio, 1.96; 95% confidence interval, 1.03–4.72).

Conclusion: The overall use of highly effective contraception at 6 weeks postpartum did not differ significantly between urban Thai women with and without GDM. However, women with GDM more frequently selected female sterilization. The use of non-highly effective contraceptive methods was similar between the two groups.

Keywords: gestational diabetes mellitus, highly effective contraception, postpartum contraception, urban women

INTRODUCTION

A short interpregnancy interval in women with recent gestational diabetes mellitus (GDM) is associated with recurrent GDM and an increased risk of type 2 diabetes mellitus (T2DM),^{1,2} leading to adverse maternal and neonatal outcomes.³⁻⁵ Effective postpartum family planning is therefore an essential component of care for women with prior GDM.⁶

Selection of an appropriate contraceptive method requires consideration of both safety and effectiveness in this high-risk population. Although some studies have reported an increased risk of T2DM after GDM among women using progestin-only hormonal contraceptive methods,^{7,8} current clinical guidelines indicate that women with a history of GDM may use the same contraceptive options as women without diabetes.⁹ Highly effective contraceptive methods, defined as female or male sterilization and long-acting reversible contraception (LARC), are recommended for women who wish to avoid short interpregnancy intervals.^{6,10}

Despite worldwide promotion of highly effective contraceptive use after pregnancies complicated by GDM, few studies have examined postpartum contraceptive practices in this population.¹¹⁻¹³ Studies from the United States have reported higher rates of female sterilization among postpartum women with GDM than among those without GDM, although findings regarding LARC use have been inconsistent.¹¹⁻¹³ These findings may not be generalizable to other settings due to socioeconomic, cultural, and geographical differences.¹⁴

Many developing countries, including Thailand, are undergoing rapid urbanization, which may influence postpartum contraceptive behaviors through differences in healthcare access, socioeconomic status, and lifestyle. In this context, the primary objective of this study was to compare the use of highly effective contraceptive methods at 6 weeks postpartum among urban Thai women with and without GDM. The use of other contraceptive methods in both groups was also examined.

MATERIALS AND METHODS

This study was approved by the Vajira Institutional Review Board (approval number 023/2564) and was performed in compliance with the Declaration of Helsinki. A cross-sectional study was conducted at the postpartum clinic of the Faculty of Medicine Vajira

Hospital. Our hospital is an 800-bed tertiary care center located in central Bangkok, the capital city of Thailand. The postpartum clinic conducts approximately 1000 postpartum visits per year.

The study included postpartum women who delivered at our institution and returned for a routine 6-week postpartum checkup between February 5, 2021, and July 7, 2021. Women aged 18 or older who had resided in the Bangkok Metropolitan area for at least 5 years and who provided written informed consent were eligible for inclusion. Women with overt diabetes or human immunodeficiency virus infection were excluded. Participants were categorized into two groups according to GDM status: women with recent GDM diagnosed using the Carpenter and Coustan criteria (GDM group) and women without GDM (non-GDM group).

The sample size was calculated based on prior study data reporting rates of highly effective contraceptive use of 20% among women with GDM and 15.7% among women without GDM.¹² With a 10% margin of error and a 95% confidence level, 62 women with GDM and 52 women without GDM were required. To account for potential exclusions, the sample size was increased by 25%, resulting in required sample sizes of 78 women with GDM and 65 women without GDM. A 1:1 matching ratio was subsequently adopted to improve statistical efficiency and simplify matching; therefore, the non-GDM group size was rounded up to 78. The final sample size of 156 participants exceeded the minimum required for the primary objective.

As part of routine clinical practice at our institution, women are scheduled to attend the postpartum clinic 6 weeks after delivery for a postpartum checkup and family planning consultation. During this visit, women receive contraceptive counseling from registered nurses or attending staff regarding available and appropriate contraceptive options. Contraceptive methods available at our clinic include LARC, such as intrauterine devices and contraceptive implants,¹³ as well as hormonal injections, oral contraceptive pills, and condoms. Other methods, including the contraceptive patch, vaginal ring, diaphragm, sponge, and spermicide, are not commonly used in Thailand and are not routinely available at our clinic.

Eligible women attending the clinic were informed about the study, and written informed consent was obtained prior to enrollment. To enhance comparability

between groups, women in the non-GDM group were matched to women in the GDM group by date of postpartum visit, parity (primiparous vs. multiparous), and gestational age at delivery (term vs. preterm).

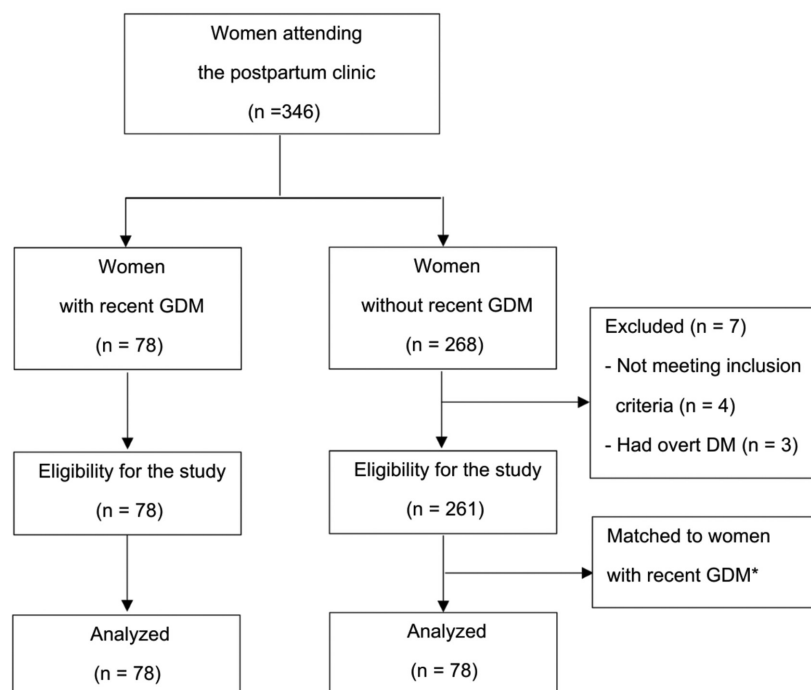
Following the routine postpartum examination and family planning services, enrolled participants completed a self-administered questionnaire, with research assistant support available as needed. The questionnaire collected information on demographic characteristics (age, education, occupation and monthly income), parity, gestational age at delivery, mode of delivery, breastfeeding practices, resumption of menstruation, prepregnancy contraceptive use, and postpartum sterilization or other contraceptive methods selected at the current visit.

Highly effective contraceptive methods included female sterilization, male sterilization, and LARC. Moderately effective methods comprised hormonal injections and oral contraceptive pills, whereas less effective methods included condoms, natural family planning, and withdrawal.¹³ Data on the lactational amenorrhea method (LAM) were also collected. LAM was defined by the presence of amenorrhea, exclusive or near-exclusive breastfeeding, and being within 6 months postpartum.¹⁵

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corporation, Armonk, NY, USA). Data are presented as numbers and percentages. Differences in participant characteristics and contraceptive methods between groups were assessed using chi-squared or Fisher's exact tests, as appropriate. Multivariable logistic regression analysis was used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for the use of highly effective contraception and female sterilization, adjusting for potential confounders including age, education, monthly income, mode of delivery, and prepregnancy contraceptive use. Statistical significance was defined as $p < 0.05$.

RESULTS

During the study period, 346 women who delivered at our institution returned for a routine 6-week postpartum checkup and family planning consultation (Figure 1). Among them, 78 had a history of GDM, whereas 268 did not. A total of 156 women were enrolled in the study, including 78 women with GDM and 78 women without GDM. Table 1 presents the demographic and obstetric characteristics of the study population. Women with GDM were significantly older



Abbreviations: DM, diabetes mellitus; GA, gestational age; GDM, gestational diabetes mellitus

Figure 1 Flow Diagram of Women Attending the Postpartum Clinic during the Study Period. *Women without recent GDM were matched to women with recent GDM in a 1:1 ratio by date of visit, parity, and GA at delivery.

Table 1 Demographic and Obstetric Characteristics of Women in the Gestational and Non-Gestational Diabetes Mellitus Groups

Characteristic	Total (n = 156)	GDM Group (n = 78)	Non-GDM Group (n = 78)	P-value
Age (years)				< 0.001
≤ 19	10 (6.4)	1 (1.3)	9 (11.5)	
20-34	114 (73.1)	48 (61.5)	66 (84.6)	
≥ 35	32 (20.5)	29 (37.2)	3 (3.9)	
Education (years)				0.337
≤ 12	121 (77.6)	58 (74.4)	63 (80.8)	
> 12	35 (22.4)	20 (25.6)	15 (19.2)	
Occupation				0.711
Employee	76 (48.7)	39 (50.0)	37 (47.4)	
Business Owner	26 (16.7)	14 (17.9)	12 (15.4)	
Public Officer	1 (0.6)	0 (0)	1 (1.3)	
Others (housewife or unemployed)	53 (34.0)	25 (32.1)	28 (35.9)	
Monthly Income				0.336
< \$ 500	97 (62.2)	46 (59.0)	51 (65.4)	
\$ 500-\$ 999	46 (29.5)	23 (29.5)	23 (29.5)	
≥ \$1000	13 (8.3)	9 (11.5)	4 (5.1)	
Parity				1.000
Primipara	50 (32.1)	25 (32.1)	25 (32.1)	
Multipara	106 (67.9)	53 (67.9)	53 (67.9)	
Gestational Age at Delivery				1.000
Term	154 (98.7)	77 (98.7)	77 (98.7)	
Preterm	2 (1.3)	1 (1.3)	1 (1.3)	
Mode of Delivery				0.193
Vaginal Delivery	92 (59.0)	42 (53.8)	50 (64.1)	
Cesarean Section	64 (41.0)	36 (46.2)	28 (35.9)	

Abbreviations: GDM, gestational diabetes mellitus; n, number

Values are reported as n (%).

than women without GDM, whereas other demographic and obstetric characteristics did not differ significantly between the two groups.

The contraceptive characteristics of the study population are presented in **Table 2**. Overall, highly effective contraceptive use was comparable between the GDM and non-GDM groups (44.9% vs. 32.1%, $p = 0.100$). Among multiparous women, approximately half (45/106) chose female sterilization. However, women in the GDM group used female sterilization at a significantly higher rate than those in the non-GDM

group (39.8% vs. 18.0%, $p = 0.003$). Male sterilization was not adopted by any participants. Regarding non-highly effective methods, the use of moderately or less effective contraceptive methods did not differ significantly between the two groups, although a higher proportion was observed in the non-GDM group (55.1% vs. 39.8%, respectively; $p = 0.054$).

Exclusive breastfeeding at the time of the study was reported by 53.8% of women in the GDM group and 51.3% in the non-GDM group ($p = 0.784$). Resumption of menstruation occurred in 5.1% of

Table 2 Contraceptive Characteristics of Women in the Gestational and Non-Gestational Diabetes Mellitus Groups

Characteristic	Total (n = 156)	GDM group (n = 78)	Non-GDM Group (n = 78)	P-value
Prepregnancy Contraceptive Use				0.745 ^a
No	64 (41.0)	31 (39.7)	33 (42.3)	
Yes	92 (59.0)	47 (60.3)	45 (57.7)	
Highly Effective Method	3 (1.9)	0 (0)	3 (3.8)	
Moderately Effective Method	84 (53.9)	44 (56.4)	40 (51.3)	
Less Effective Method	5 (3.2)	3 (3.9)	2 (2.6)	
Postpartum Contraceptive Use				0.360 ^b
No Contraception	7 (4.5)	3 (3.8)	4 (5.1)	
Highly Effective Method	60 (38.5)	35 (44.9)	25 (32.1)	
Female Sterilization	45 (28.9)	31 (39.8)	14 (18.0)	
Male Sterilization	0 (0)	0 (0)	0 (0)	
Intrauterine Device	2 (1.3)	0 (0)	2 (2.6)	
Implant	13 (8.3)	4 (5.1)	9 (11.5)	
Moderately Effective Method	67 (42.9)	28 (35.9)	39 (50.0)	
Hormonal Injection	40 (25.6)	16 (20.5)	24 (30.8)	
Pill	27 (17.3)	12 (15.4)	15 (19.2)	
Less Effective Method	7 (4.5)	3 (3.9)	4 (5.1)	
Condom	6 (3.9)	2 (2.6)	4 (5.1)	
Natural Family planning/withdrawal	1 (0.6)	1 (1.3)	0 (0)	
LAM	15 (9.6)	9 (11.5)	6 (7.7)	

Abbreviations: GDM, gestational diabetes mellitus; LAM, lactational amenorrhea method; n, number

Values are reported as n (%).

^a Comparison of the presence and absence of prepregnancy contraceptive use.

^b Comparisons among no contraception, highly effective, moderately effective, less effective contraceptive methods, and LAM.

women with GDM and 14.1% of women without GDM ($p = 0.057$). The proportions of women using the LAM as a sole temporary contraceptive method were 11.5% in the GDM group and 7.7% in the non-GDM group ($p = 0.415$), while no contraception was reported by 3.8% and 5.1% of women, respectively ($p = 0.699$).

Multivariable logistic regression analysis adjusted for potential confounders, including age, education, monthly income, mode of delivery, and prepregnancy contraceptive use, demonstrated no independent association between GDM and the overall use of highly effective contraceptive methods at 6 weeks postpartum (Table 3). However, GDM was independently associated

Table 3 Multivariable Logistic Regression Analyses for the Associations of Gestational Diabetes Mellitus Status with Overall Use of Highly Effective Contraceptive Methods and Use of Female Sterilization at 6 Weeks Postpartum

Variable	Highly Effective Contraceptive use ^a		Female Sterilization ^b	
	Crude OR (95% CI)	aOR ^c (95% CI)	Crude OR (95% CI)	aOR ^c (95% CI)
GDM Status				
No	Reference	1.00	Reference	1.00
Yes	1.72 (0.90-3.31)	1.18 (0.54-2.56)	3.02 (1.45-6.29)	1.96 (1.03-4.72)
Age (years)				
≤ 19	0.46 (0.09-2.28)	0.48 (0.09-2.58)	–d	–d
20-34	Reference	1.00	Reference	1.00
≥ 35	2.38 (1.07-5.28)	1.97 (0.78-4.97)	3.48 (1.54-7.86)	2.43 (0.92-6.41)
Education (years)				
≤ 12	Reference	1.00	Reference	1.00
> 12	0.79 (0.36-1.74)	0.55 (0.22-1.35)	0.67 (0.28-1.62)	0.38 (0.13-1.11)
Monthly Income				
< \$ 500	Reference	1.00	Reference	1.00
\$ 500-\$ 999	1.25 (0.61-2.56)	1.57 (0.71-3.48)	1.20 (0.55-2.59)	1.62 (0.66-4.01)
≥ \$ 1000	1.52 (0.47-4.88)	1.61 (0.42-6.19)	1.71 (0.51-5.69)	1.78 (0.42-7.65)
Mode of Delivery				
Vaginal Delivery	Reference	1.00	Reference	1.00
Cesarean Section	3.23 (1.65-6.34)	3.59 (1.75-7.38)	3.94 (1.90-8.17)	4.79 (2.11-10.87)
Pregnancy Contraceptive Use				
No	Reference	1.00	Reference	1.00
Yes	1.69 (0.87-3.31)	1.89 (0.91-3.93)	1.82 (0.87-3.78)	1.93 (0.84-4.47)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; GDM, gestational diabetes mellitus; OR, odds ratio. Values are reported as n (%).

^a Versus use of non-highly effective methods or no method.

^b Versus use of reversible contraceptive methods or no method.

^c Adjusted for the other variables in the table.

^d No woman in this age group underwent female sterilization.

with female sterilization (aOR 1.96, 95% CI 1.03–4.72). Cesarean section (CS) was independently associated with both the overall use of highly effective contraception (aOR 3.59, 95% CI 1.75–7.38) and female sterilization (aOR 4.79, 95% CI 2.11–10.87).

DISCUSSION

This study evaluated contraceptive practice at 6 weeks postpartum among urban women with and without recent GDM. We focused on contraceptive practice at this time point because it coincides with routine postpartum follow-up and family planning counseling. At this early postpartum stage, women who do not undergo sterilization at delivery may consider other highly effective contraceptive options, including LARC and male sterilization, which are associated with failure rates of less than 1%.¹⁶

Our findings indicate that the overall use of highly effective contraceptive methods did not differ significantly between women with and without GDM. However, women with GDM were significantly more likely to choose female sterilization. Multivariable analysis confirmed that GDM was independently associated with female sterilization but not with overall uptake of highly effective contraception. Additionally, cesarean delivery was independently associated with both outcomes.

The overall prevalence of highly effective contraceptive use in our cohort (38.5%) was higher than the 17.1–29.8% reported in prior questionnaire-based surveys of postpartum women with and without diabetes in the United States.^{11–13} Despite this higher overall rate, our finding that GDM was not associated with increased overall use of highly effective contraception contrasts with results from Morris et al.,¹³ who reported greater uptake among women with diabetes. Several factors may contribute to this variation, including differences in study design, population characteristics (age, parity, education, and income), and timing of assessment. While Morris et al. evaluated contraceptive practice at 2–4 months postpartum, our study focused specifically on the 6-week postpartum visit. Contraceptive decisions may evolve over time during the postpartum period, and early postpartum choices may not reflect longer-term contraceptive patterns. Beyond timing differences, the specific methods chosen also varied between populations.

The distribution of specific contraceptive methods in our study also differed from earlier reports.^{12,13}

Female sterilization was the predominant highly effective method in our cohort, whereas LARC was more commonly used in prior American population-based studies.^{12,13} Although multiparity was frequent (67.9%) in our population, a similarly high proportion of women with one or more prior live births (58.7%) was reported in an earlier study,¹³ suggesting that parity alone is unlikely to account for differences in method distribution. Differences in healthcare systems, cultural norms, reproductive intentions, and accessibility of contraceptive services may partly explain these discrepancies.

Although overall highly effective contraceptive use did not differ by GDM status, the higher rate of female sterilization among women with GDM is consistent with several previous survey-based studies conducted in the United States,^{11–13} although the magnitude of association has varied across populations. This finding may reflect differences in perceived future pregnancy risks or completed family size preferences rather than the presence of GDM itself. However, because our study did not evaluate reproductive intentions, perceived pregnancy risk, or decision-making processes, the reasons underlying contraceptive selection cannot be determined from these data.

Similar to findings regarding overall highly effective contraceptive use, we did not observe a significant association between GDM and LARC use, which is consistent with two earlier reports.^{11,13} The use of moderately or less effective contraceptive methods tended to be higher among women without GDM, although this difference was not statistically significant. These patterns may reflect variations in individual preferences, reproductive goals, or counseling uptake; however, firm conclusions cannot be drawn in the absence of direct measures of these factors.

Beyond GDM status, cesarean delivery was independently associated with both female sterilization and the overall use of highly effective contraception. This association has been described previously and may partly reflect the opportunity to perform sterilization concurrently with cesarean delivery, which can directly influence the immediate postpartum contraceptive choice.¹³ In addition, cesarean delivery is associated with increased risks in subsequent pregnancies, including uterine rupture, placenta previa, and placenta accreta.¹⁷ Awareness of these risks may lead some women to prefer highly effective contraceptive methods in order to avoid or delay future pregnancies.

This study has several strengths. Data were

collected prospectively at the time of postpartum examination and contraceptive counseling, minimizing recall bias and reliance on retrospective recall. Matching women without GDM to women with GDM improved comparability between groups. The use of a predefined definition of urban residence allowed focused evaluation of a stable urban population.¹⁸ In addition, collection of LAM data reduced the likelihood of misclassification of contraceptive status.

Several limitations should be acknowledged. The study was conducted at a single urban tertiary care center, which may limit generalizability to rural populations or other healthcare settings. Women relying on LAM were not followed longitudinally, and subsequent contraceptive transitions were not captured. The sample size was determined based on the primary objective and may have limited statistical power to detect associations with less common outcomes such as male sterilization or LARC use. We were also unable to measure the content or intensity of postpartum contraceptive counseling, which may influence contraceptive decision-making.^{19,20} Because of the cross-sectional design, these findings represent associations observed at a single postpartum time point and should not be interpreted as causal relationships.

CONCLUSION

In conclusion, contraceptive practices at 6 weeks postpartum among urban women with GDM were not significantly different from those among women without GDM, except for a higher rate of female sterilization in the GDM group. Future studies with larger sample sizes and longer follow-up periods are needed to evaluate postpartum contraceptive continuation, method switching, and subsequent pregnancy outcomes among women with and without GDM.

Conflict of Interest

The authors declare no conflict of interest.

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Author Contributions

Conceptualization: A.P., C.P.

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Formal analysis: C.P.

Funding acquisition: C.P.

Investigation: A.P., C.P.

Methodology: C.P.

Project administration: -

Resources: -

Software: -

Supervision: C.P.

Validation: A.P., C.P.

Visualization: -

Writing – original draft preparation: A.P., C.P.

Writing – review & editing: A.P., C.P.

Data Availability Statement

Data are available upon reasonable request.

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ORIGINAL ARTICLE

Halving Sugar Intake Increases Sweet Taste Intensity in Thai Adults with Moderate to High Sugar Consumption: A Randomized Controlled Trial

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ABSTRACT

Objectives: To determine whether a 50% reduction in daily sugar intake increases sweet taste intensity among Thai adults, and whether changes in taste perception and dietary sugar intake persist after the restriction period ends.

Materials and Methods: A randomized, double-blind, controlled trial was conducted over 12 weeks among 52 healthy Thai adults. Participants were assigned to either a sugar-reduction group instructed to halve their daily sugar intake ($n = 25$) or a control group that maintained their usual diet ($n = 27$). Sweet taste intensity was evaluated using the general labeled magnitude scale at baseline, week 16 (end of restriction), and week 24 (after resumption of regular diet). The primary outcome was the proportion of participants with increased sweet taste intensity at week 16, while secondary outcomes included sweet taste intensity at week 24 and changes in dietary sugar intake.

Results: At week 16, significantly more participants in the intervention group reported heightened sweet taste intensity compared with the control group (64% vs 33.3%, $p = 0.027$). After participants resumed their usual diets at week 24, this difference was no longer statistically significant (44% vs 38.5%, $p = 0.688$). Dietary sugar intake significantly decreased during the intervention period, but partially rebounded after restriction was lifted. No significant between-group differences were observed in total energy intake or anthropometric outcomes.

Conclusion: A 12-week 50% sugar-reduction intervention increased sweet taste intensity. However, both taste perception and dietary behaviors partially reverted after the restriction was lifted, suggesting that sensory adaptation alone may not sustain long-term change.

Keywords: dietary modification, dietary sugars, noncommunicable diseases, sugar reduction, taste perception

INTRODUCTION

Noncommunicable diseases (NCDs), including cardiovascular disease, diabetes, hypertension, and cancer, are the leading causes of mortality worldwide, accounting for more than 40 million deaths each year.¹ In Thailand, NCDs are responsible for over three-quarters of all deaths, with nearly 400,000 deaths reported annually.^{2,3} Excess dietary sugar intake, particularly from sugar-sweetened beverages, represents a major modifiable risk factor.⁴ Although global sugar consumption averages 22.1 kg per person annually,⁵ Thai adults consume about 25 teaspoons per day, nearly four times the WHO recommendation, despite the implementation of a national sugar tax.^{6,7}

Reducing dietary sugar intake is a cornerstone of NCD prevention. WHO guidelines recommend limiting sugar intake to < 10% of daily energy, with a conditional target of < 5%.⁸ Beyond its direct caloric effects, gradual sugar reduction may recalibrate sweet taste perception, promoting lower-sugar habits. Controlled trials in Western populations have shown that reducing dietary sugar increases sweet taste intensity,⁹ potentially mediated by up regulation of sweet taste receptors such as T1R2/T1R3.¹⁰ However, the persistence of this adaptation once restriction is lifted remains uncertain and evidence from high-sugar environments such as Thailand is scarce.

This study aimed to evaluate whether a 50% reduction in daily sugar intake among Thai adults increases sweet taste intensity, whether the effect persists after restriction ends, and whether the intervention alters dietary sugar intake.

MATERIALS AND METHODS

This study was conducted as a randomized controlled trial among healthy Thai adults between October 2024 and June 2025. The study protocol, titled "Alteration of sweet taste perception after 50% reduction of sweet food and beverage consumption for 12 weeks, compared with unmodified diet," was approved by the Siriraj Institutional Review Board (COA no. Si 456/2024) and registered at ClinicalTrials.gov (NCT06678386). All participants provided written informed consent prior to enrollment, and all procedures adhered to the Declaration of Helsinki and Good Clinical Practice guidelines.

Eligible participants were adults aged 18–59 years with fasting blood glucose < 126 mg/dL or HbA1c < 6.5% within the previous six months, and a Sweet

Food Consumption Behavior Questionnaire score ≥ 10 , indicating high risk of excessive sweet intake.¹¹ Individuals with uncontrolled chronic disease, severe illness, pregnancy, daily medication use (except contraceptives or vitamins), or $\geq 10\%$ unintentional weight change within the past three months were excluded.

Randomization was performed using computer-generated blocks of four, with assignment concealed in sealed opaque envelopes until baseline assessment. Due to the nature of the intervention, dietitians and participants were not blinded to group allocation. Sweet taste testing, however, was conducted under double-blind conditions. Sucrose solutions (5%, 10%, 15%, 20%, and water) were coded and presented in random order by independent staff, ensuring both participants and assessors remained unaware of solution concentrations during testing.

Participants in the intervention group received individualized dietary counseling at week 4, which included tailored feedback on habitual dietary patterns and strategies to reduce added sugar in food and beverages. From weeks 5 to 16, participants were instructed to reduce daily sugar intake by 50%. Compliance was assessed through 3-day food records and photographic dietary logs submitted online at weeks 1, 5, 10, 16, and 24. Control participants were instructed to maintain their usual diets for the duration of the intervention. From weeks 17 to 24, both groups resumed unrestricted dietary intake.

The primary outcome was the proportion of participants who demonstrated increased sweet taste intensity at week 16 compared with baseline. Secondary outcomes included the proportion with increased sweet taste intensity at week 24, changes in daily sugar intake, anthropometric measures (weight, body mass index (BMI), waist circumference), and self-reported sweet consumption behaviors. Sweet taste intensity was assessed using the general labeled magnitude scale (gLMS)^{12,13}; the scale template is provided in the Supplementary Material, with video instructions provided before each testing session. Dietary sugar intake was evaluated using 3-day food records corroborated by participant-submitted photographs.

The sample size was calculated to detect a 30% increase in sweet taste intensity in the intervention group versus a 2% increase in the control group, assuming $\alpha = 0.05$ and power = 80%. A minimum of 26 participants per group was required, and the target sample was increased to 58 to account for an

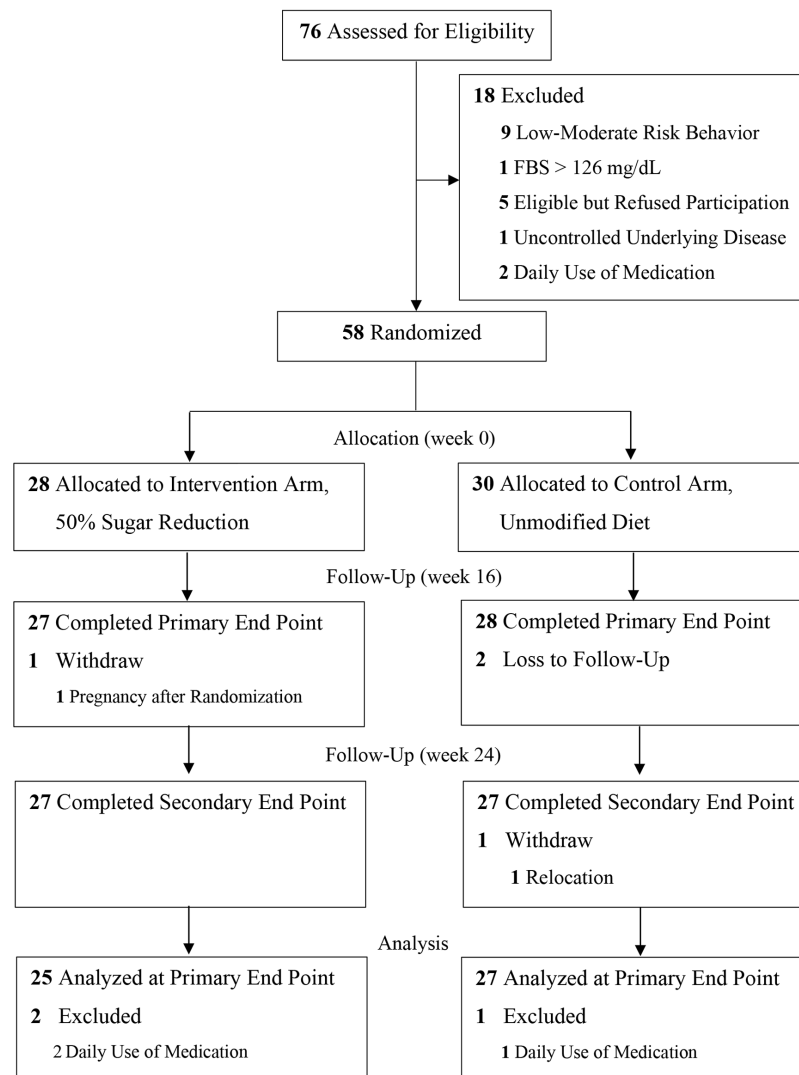
anticipated 10% attrition rate.

Baseline characteristics were compared using independent T-tests for continuous variables and Chi-square tests for categorical variables. Proportions of participants with increased sweet taste intensity at weeks 16 and 24 were analyzed using Chi-square tests. Repeated-measure continuous outcomes, including daily sugar intake, were analyzed using generalized estimating equations with an exchangeable correlation structure to account for within-subject correlations. Bonferroni correction was applied for multiple comparisons. Analyses followed a modified intention-to-treat approach, excluding only those later identified as ineligible after randomization. Results are presented as estimated means with standard errors, with statistical significance defined as $p < 0.05$.

RESULTS

A total of 76 individuals were screened, of whom 58 were randomized (28 in the intervention group and 30 in the control group). At the primary endpoint, 55 participants completed follow-up, with minimal attrition: one due to pregnancy and two lost to follow-up. By the secondary endpoint, 54 participants completed the study, with one participant relocating. Three participants who reported daily medication use were excluded prior to analysis, resulting in a final analysis set of 52 participants. (Figure 1)

Baseline characteristics of the analysis set ($n = 52$) are summarized in Table 1. The mean age was 33.5 ± 7.5 years, and the mean BMI was 23.7 ± 4.0 kg/m², with the majority being female (94.2%). No significant differences were observed between groups



Abbreviations: dL, deciliter; FBS, fasting blood sugar; mg, milligrams

Figure 1 Study Flow Diagram of Participant Recruitment, Randomization, and Follow-Up

Table 1 Baseline Characteristics of Participants

Variables	Control (n = 27)		Intervention (n = 25)		P-value ^a
	n	%	n	%	
Sex					0.507
Female	26	96.3	23	92.0	
Male	1	3.7	2	8.0	
Age, years, mean $\pm$ SD	33.37 $\pm$ 7.54		33.76 $\pm$ 7.47		0.852
BW, kg, mean $\pm$ SD	60.32 $\pm$ 11.30		60.66 $\pm$ 10.78		0.911
BMI, kg/m ² , mean $\pm$ SD	24.15 $\pm$ 4.20		23.32 $\pm$ 3.81		0.457
WC, cm, mean $\pm$ SD	81.41 $\pm$ 9.90		80.36 $\pm$ 8.61		0.687
FBS, mg/dL, mean $\pm$ SD	91.63 $\pm$ 8.40		94.32 $\pm$ 6.32		0.201
Underlying disease ^b					0.515
Yes	5	18.5	3	12.0	
No	22	81.5	22	88.0	
Smoking					0.956
Quit	1	3.7	1	4	
Never use	26	96.3	24	96.0	
Alcohol drinking					0.701
Current use	7	25.9	6	24.0	
Quit	4	14.8	6	24.0	
Never use	16	59.3	13	52.0	
Exercise ^c					0.186
Yes	4	14.8	1	4.0	
No	23	85.2	24	96.0	
Sweet consumption behavior ^d					0.884
Very high risk behavior	1	3.7	1	4.0	
High risk behavior	19	70.4	16	64.0	
Moderate risk behavior	7	25.9	8	32.0	

Abbreviations: BMI, body mass index; BW, body weight; cm, centimeter; dL, deciliter; FBS, fasting blood sugar; kg, kilogram; m², square meter; mg, milligrams; n, number; SD, standard deviation; WC, waist circumference

^a Statistically significant at $p < 0.05$ (independent T-test for continuous variables; Chi-square test for categorical variables).

^b Self-reported underlying diseases: participants reported having anemia, polycystic ovarian syndrome, allergic rhinitis or gastroesophageal reflux, and were taking vitamins, oral contraceptives, or intermittent medications to relieve symptoms.

^c Exercise: "Yes" indicates ≥ 150 minutes/week; "No" indicates < 150 minutes/week

^d Sweet consumption behavior was assessed using the sweet food consumption behavior questionnaire: appropriate intake (score < 5), moderate risk (6–9), high risk (10–13), very high risk (14–15). All participants scored ≥ 10 during eligibility screening; scores may have changed at baseline assessment.

in age, anthropometric measures (BMI, body weight, waist circumference), fasting blood sugar, or sweet consumption behaviors (all $p > 0.05$).

At week 16, a significantly greater proportion of participants in the intervention group reported increased sweet taste intensity compared with the control group (64% vs 33.3%, $p = 0.027$; **Table 2**). By week 24,

after both groups had resumed their usual diets, the difference was no longer significant (44% vs 38.5%, $p = 0.688$). The distribution of stepwise changes in sweet taste intensity at weeks 16 and 24 is shown in **Table 3**.

Daily sugar calorie intake decreased significantly in the intervention group during the 12-week intervention

Table 2 Proportion of Participants by Change in Sweet Taste Intensity

Change in Sweet Taste Intensity	Control		Intervention		P-value
	n	%	n	%	
At week 16					
Increased ^a	9	33.3	16	64.0	0.027
Not increased	18	66.7	9	36.0	
At week 24					
Increased ^a	10	38.5	11	44.0	0.688
Not increased	16	61.5	14	56.0	

^a Proportion of participants with increased sweet taste intensity at week 16 (primary outcome) and at week 24 (secondary outcome) compared with baseline. Statistical significance was assessed using Chi-square test ($p < 0.05$).

Table 3 Distribution of Stepwise Changes in Sweet Taste Intensity at Weeks 16 and 24 by Study Group

Change in Sweet Taste Intensity	Control		Intervention	
	n	%	n	%
At week 16				
3-steps increase	1	3.7	1	4.0
2-steps increase	1	3.7	1	4.0
1-step increase	7	25.9	8	32.0
No change	14	51.9	14	56.0
1-step decrease	3	11.1	1	4.0
2-steps decrease	1	3.7	1	4.0
At week 24				
3-steps increase	1	3.8	0	0
2-steps increase	7	26.9	4	16.0
1-step increase	8	30.8	7	28
No change	7	26.9	11	45.8
1-step decrease	2	7.7	1	4.0
2-steps decrease	0	0	2	0

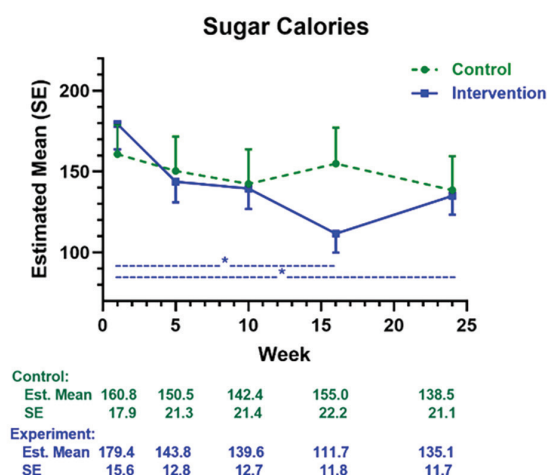
and partially rebounded after diet normalization (**Figure 2**). Within-group analysis revealed significant reductions at both week 16 ($p < 0.001$) and week 24 ($p = 0.019$) relative to baseline. Between-group comparisons revealed the largest difference at week 16, with the intervention group consuming 43.26 kcal/day less than the control group ($p = 0.085$). By week 24, this difference was minimal (-3.39 kcal/day, $p = 0.888$).

Additional outcomes, including total energy intake, anthropometric data, and self-reported sweet consumption behaviors, are provided in the supplementary materials. The estimated mean difference in total energy intake at week 16 was -17.52 kcal/day ($p = 0.803$). Both groups reported significant within-group reductions

in sweet consumption behaviors at weeks 16 and 24 compared with baseline, however, between-group differences were not statistically significant.

DISCUSSION

This trial found that reducing dietary sugar intake by 50% for 12 weeks significantly increased perceived sweet taste intensity. These findings suggest that real-world sugar reduction can shift sensory sensitivity to sweetness. However, once dietary restriction ended, the effect diminished rapidly, indicating that sensory adaptation is short-lived in the absence of continued reinforcement.



Abbreviations: Est mean, estimated mean; SE, standard error

Figure 2 Estimated Mean Daily Sugar Calories from Baseline to Week 24 by Study Group

Our results are consistent with those of Wise et al.,⁹ who reported increased sweet taste perception following sugar reduction in a Western population. The transient reversal observed in our study mirrors that finding, supporting the notion that sensory adaptation is robust but temporary. Notably, our trial extends this evidence to an Asian population regularly exposed to a high-sugar food environment with hidden sugars in sauces, street foods, and beverages,⁶ demonstrating the generalizability of this phenomenon across cultural contexts.

The novelty of our study lies in its focus on participants with high sugar exposure. Despite this challenging baseline, participants achieved measurable sensory adaptation, suggesting that even partial reduction can influence perception. However, although participants were instructed to reduce sugar intake by 50%, the observed reduction in daily sugar calories was lower than planned, reflecting real-world adherence challenges. This partial adherence may have attenuated both the magnitude and durability of sensory adaptation, highlighting the potential importance of continued behavioral support and follow-up to sustain dietary change. Whether greater or longer reductions in sugar intake could lead to more sustained changes in sweet taste perception or delay rebound remains unclear and warrants further investigation.

Strengths of this study include its randomized

design, blinded outcome assessment, and use of validated dietary and taste measures. The intervention reduced sugar intake by 43 kcal/day (11 g, 3 teaspoons), which could yield health benefits if sustained. Nonetheless, total caloric intake did not change, suggesting caloric compensation from other nutrients, a pattern reported in prior literature.¹⁴ Limitations include modest sample size, predominance of female participants (94%), reliance on self-reported dietary data, and short intervention period. Additionally, a modified intention-to-treat analysis was performed to avoid bias from ineligible participants.

CONCLUSION

Halving sugar intake for 12 weeks increased sweet taste intensity. However, both taste perception and dietary behaviors partially reverted after the restriction was lifted, suggesting that sensory adaptation alone may not sustain long-term dietary change.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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 Funding acquisition: N.S., T.N.
 Investigation: N.S., M.C., W.P., W.C.
 Methodology: T.N., W.P.
 Project administration: N.S., T.N.
 Resources: N.S., T.N.
 Software: N.S., T.N.
 Supervision: T.N.
 Validation: N.S., T.N.
 Visualization: N.S., T.N.
 Writing – original draft preparation: N.S., T.N.
 Writing – review & editing: T.N.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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ORIGINAL ARTICLE

Effect of Vitamin D Supplementation in Healthy Full-Term Infants: A Randomized, Double-Blind, Placebo-Controlled Trial

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ABSTRACT

Objectives: Vitamin D deficiency in infants is a significant global health issue. The aim of this randomized, double-blind, placebo-controlled trial was to assess the effectiveness of vitamin D supplementation in infants at 6 months of age in preventing deficiency or promoting sufficient vitamin D status.

Materials and Methods: Sixty-eight healthy full-term infants were randomly assigned to receive either vitamin D supplementation, 400 international unit (IU)/day (intervention group; n = 34), or placebo (control group; n = 34). Blood samples were collected 48–72 hours after birth to measure serum 25-hydroxyvitamin D (25(OH)D) levels. Supplementation began after blood collection and continued for 6 months. The serum 25(OH)D levels of the two groups were then compared.

Results: After six months, vitamin D supplementation significantly increased mean serum 25(OH)D levels by 7.07 nanograms per milliliter compared to placebo (95% confidence interval (CI): 1.30–12.83; p = 0.016). Among breastfed infants, supplementation with vitamin D 400 IU/day resulted in significantly improved vitamin D status. Notably, 100% of infants in the intervention group achieved vitamin D sufficiency, compared to 77.8% in the control group (p = 0.046). Furthermore, supplemented breastfed infants exhibited significantly higher mean serum 25(OH)D levels at six months (p = 0.019) and a greater increase from baseline (p = 0.010) relative to the control group. In contrast, these effects of supplementation were not observed among formula-fed or mixed-fed infants.

Conclusion: This study highlights the high prevalence of vitamin D insufficiency and deficiency among healthy Thai neonates. Daily supplementation with 400 IU of vitamin D from birth to age 6 months among breastfed infants significantly improved the prevalence of vitamin D sufficiency and elevated serum vitamin D levels by age 6 months without any adverse effects.

Keywords: infant, placebo, randomized controlled trial, vitamin D

INTRODUCTION

Vitamin D deficiency and rickets in infancy are recognized as significant global health problems.^{1,2} The prevalence of vitamin D insufficiency or deficiency in the cord blood of newborns ranges from 20.2% to 69.1%; contributing factors include low maternal serum 25-hydroxyvitamin D (25(OH)D) levels and a lack of vitamin D supplementation during pregnancy.³

Infants are particularly vulnerable to vitamin D deficiency because human breast milk contains low levels of vitamin D (15–50 international unit (IU)/liter (L)), which are insufficient for meeting the daily vitamin D requirements of breastfed newborns.^{4,5} Even formula-fed infants who consume approximately 750 (milliliter) mL/day of vitamin D-fortified formula may receive less than the recommended daily intake of 400 IU/day.^{6–8} In addition, inadequate sunlight exposure during infancy further exacerbates the risk of vitamin D insufficiency or deficiency; thus, supplementation is needed.

Numerous studies have supported the recommendation of supplementing both breastfed and formula-fed infants with 400 IU/day of vitamin D for at least the first 6 months of life.^{9–13} According to international guidelines, 400 IU/day of vitamin D should be administered to all infants, starting within the first few days of life and continuing for 1 year or until the infant consumes at least 1 L per day of vitamin D-fortified formula or whole milk.^{14–16} Despite these global recommendations, routine vitamin D supplementation is not widely supplied to healthy infants in Thailand. The possible reasons include the lack of national guidelines on vitamin D supplementation and the limited availability of studies demonstrating its efficacy in Thai infants.¹⁷

The aim of this study was to evaluate the effectiveness of vitamin D supplementation in preventing deficiency or achieving sufficient levels in breastfed and formula-fed Thai infants by the age of 6 months.

MATERIALS AND METHODS

This randomized, double-blind, placebo-controlled study was conducted at Vajira Hospital, Bangkok, Thailand, between July 16, 2020, and September 22, 2021. The study protocol was approved by the Institutional Review Board of the Faculty of Medicine Vajira Hospital (COA 142/2562, October 24, 2019) and was registered retrospectively in the Thai Clinical Trials Registry (thaiclinicaltrial.org; TCTR20240405002)

on April 5, 2024. This study adhered to the Consolidated Standards of Reporting Trials criteria for parallel-group randomized trials.

The sample size was determined to detect a difference in the prevalence of vitamin D sufficiency at 6 months of age between the intervention and placebo groups. At the time the study protocol was developed, no data were available on the prevalence of vitamin D deficiency among 6-month-old Thai infants or from randomized trials evaluating vitamin D supplementation in this population. Therefore, estimates were derived from previously published studies. Data from the South East Asian Nutrition Surveys indicated that vitamin D sufficiency was present in 54.4% of urban Thai children who had not received vitamin D supplementation.¹⁸ For the intervention group, we used data from a study of Turkish infants receiving 400 IU/day of vitamin D supplementation, in which 88% of infants were vitamin D sufficient.¹⁹ This population was considered comparable to our cohort because it included both breastfed and formula-fed infants. Based on these assumptions, a minimum sample size of 28 infants per group was required to achieve 80% power with a two-sided significance level of 0.05. To allow for an anticipated 20% loss to follow-up, the final target sample size was increased to 34 infants per group.

In accordance with the declaration of Helsinki, we required all mothers to give written informed consent to participate before their inclusion in the study. Eligible participants were healthy infants born at Vajira Hospital at full term (gestational age, 37–42 weeks), at normal birth weight (2500–4000 gram), and with no perinatal asphyxia (Apgar score at 5 minutes, > 7), and whose mothers were 18–35 years of age and had no known medical disorders. We excluded newborns receiving medications that affect vitamin D levels (e.g., steroids and antiepileptic drugs) and those with diagnosed intrauterine growth retardation, chromosomal abnormalities, congenital anomalies, or sepsis.

Randomization was performed when infants were 48–72 hours old using a computer-generated block of four by one author (R.P.). Parents and clinicians involved in enrollment, data collection, and analysis (S.T. and T.T.) were blinded to group allocation. At study initiation, no commercially available vitamin D syrup was available in Thailand; therefore, the study medication was compounded in-house by a

hospital pharmacist (R.P.). To maintain double blinding, vitamin D and placebo syrups were prepared in identical 50-mL opaque bottles and were indistinguishable in appearance. The vitamin D syrup (400 IU/mL) was prepared by dissolving calciferol capsules (vitamin D₂, 20,000 IU) in 50 mL of 70% glucose in water, while the placebo consisted of dextrose powder dissolved in the same solution. The compounded preparations were stable at room temperature with an in-use stability of 45 days. As infants were followed up every two months, parents received two bottles at each visit: one prepared by the pharmacist for the first month and pre-measured vitamin D or placebo powder with 70% glucose solution for self-preparation during the second month, following standardized instructions.

We assessed baseline maternal and infant data that could influence serum vitamin D levels, including skin color, duration of sun exposure, sunscreen use, vitamin D intake and supplementation, type of feeding, and season of birth. Skin color in nonexposed areas (e.g., the inner arm or abdomen) of mothers and infants was assessed via the Fitzpatrick skin type classification.²⁰ The duration of sun exposure was assessed by asking mothers to report the average daily time (in minutes) that both the mother and infant were exposed to sunlight between 9:00 a.m. and 3:00 p.m., the period during which cutaneous vitamin D synthesis is most effective. Sunscreen use was evaluated by asking mothers whether they routinely used sunscreen. Maternal vitamin D intake and supplementation included vitamin D obtained from both single-ingredient vitamin D supplements and combined or multivitamin preparations containing vitamin D.

After 1 mL of venous blood was collected from mothers and their infants to measure baseline serum 25(OH)D levels, the infants were given 1 mL of either vitamin D or placebo syrup daily, according to their assigned group, until they were 6 months of age. In accordance with hospital policy, all mothers were encouraged to exclusively breastfeed their infants, as this was the optimal method of feeding. When exclusive breastfeeding was not feasible, mixed feeding or formula feeding was allowed as an alternative. Solid foods were introduced when infants were between the ages of 4 and 6 months.

At 2, 4, and 6 months of age, the infants visited the pediatric outpatient clinic, Vajira Hospital, for routine immunizations, growth assessments

(including weight and length), evaluation of adherence to the supplementation regimen, and monitoring of potential adverse events related to vitamin D toxicity (e.g., symptoms of hypercalcemia, such as nausea, vomiting, constipation, polydipsia, polyuria, muscle weakness, and twitching). At each visit, mothers were provided with two bottles of either vitamin D or placebo syrup. When infants were 6 months of age, we collected 2 mL of their venous blood to assess the serum levels of 25(OH)D, intact parathyroid hormone (PTH), alkaline phosphatase, calcium, and phosphorus to evaluate vitamin D status and adverse events related to supplementation.

Infants who did not complete the study included those who experienced adverse effects from vitamin D supplementation and those whose parents withdrew from the study or did not adhere to the research protocol, such as due to difficulty administering the supplement or inability to attend follow-up visits. To ensure participant safety, an interim analysis was conducted after 50% of participants in each group had been enrolled, and a progress report was subsequently submitted to the Ethics Committee. Serum 25(OH)D and intact PTH concentrations were measured using electrochemiluminescence immunoassays (Elecys Vitamin D total II assay and Elecys PTH assay on the cobas® 8000 e 801 analytical unit; Roche Diagnostics, Basel, Switzerland).²¹ Serum calcium, phosphorus, and alkaline phosphatase levels were measured using photometric methods (cobas® pro integrated solutions c 503 analytical unit; Roche Diagnostics, Mannheim, Germany). Internal quality controls were included in each assay batch to ensure accuracy and precision. Vitamin D status was categorized according to serum 25(OH)D levels as follows: deficiency, < 12 nanograms (ng)/mL (< 30 nmol (nanomoles)/L); insufficiency, 12–20 ng/mL (30–50 nmol/L); and sufficiency, > 20 ng/mL (> 50 nmol/L).¹⁴

The primary outcome of this study was the effect of vitamin D supplementation on the prevalence of vitamin D sufficiency among 6-month-old infants in the intervention and control groups. The secondary outcome was the effect of vitamin D supplementation on serum 25(OH)D level in 6-month-old infants fed breast milk, infant formula and mixed feeding.

We used Stata 13 (StataCorp, College Station, TX, United States) to perform statistical analyses. Data for continuous variables were calculated as means ± standard deviations. To compare the two groups,

we used the independent t test or the Mann-Whitney U test, depending on the data distribution. Data for categorical variables were calculated as counts and percentages, and we compared the groups by using the Chi-square test or Fisher's exact test, as appropriate.

We performed per-protocol analysis to evaluate the effect of vitamin D supplementation on the prevalence of vitamin D sufficiency at age 6 months in comparison with baseline levels in both the intervention and control groups. We conducted multilevel Poisson regression with random intercepts and fixed effects to evaluate and compare the prevalence ratios of vitamin D sufficiency at age 6 months in the two groups. Furthermore, we used multilevel linear regression with random intercepts and fixed effects to analyze the mean differences in serum 25(OH)D levels at baseline between the two groups and from baseline to 6 months within both groups, as well as the mean difference in serum 25(OH)D level changes between the two groups. A p-value of < 0.05 was considered statistically significant.

RESULTS

Among the 68 participants initially enrolled and randomly assigned to receive either vitamin D syrup (intervention group; $n = 34$) or placebo syrup (control

group; $n = 34$), 3 participants from the intervention group and 4 from the control group were withdrawn from the study or lost to follow-up. In addition, the parents of 2 participants from each group did not comply with the supplementation regimen. We therefore analyzed the data of the 57 infants (83.8%) who completed the 6-month study. (**Figure 1**)

The characteristics of mothers and infants in the two groups at baseline did not differ significantly. The baseline serum 25(OH)D levels and vitamin D status of mothers in the two groups were comparable. At 6 months of age, infant feeding practices, duration of sun exposure, type of feeding, growth parameters, and serum levels of calcium, phosphorus, alkaline phosphatase, and intact PTH in the two groups were similar. None of the infants had hypercalcemia or adverse events related to vitamin D toxicity during the study. (**Table 1**)

Table 2 demonstrated the effect of vitamin D supplementation on the prevalence of vitamin D sufficiency and mean serum 25(OH)D of infants at six months. The prevalence of vitamin D sufficiency among the infants at 6 months of age increased significantly from baseline in both the intervention group ($p = 0.002$) and the control group ($p = 0.044$). Although this

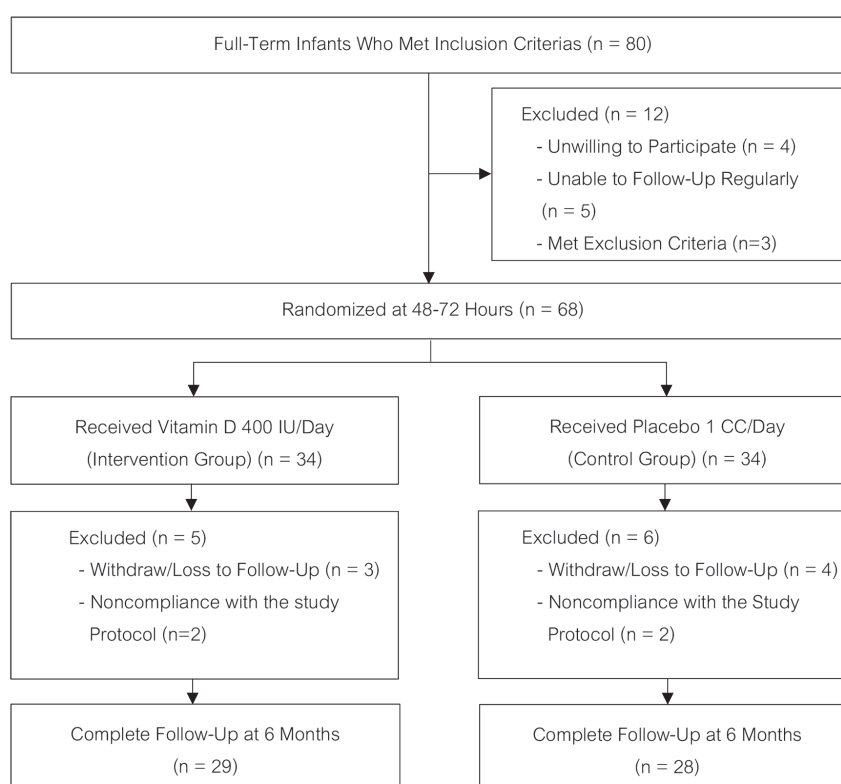


Figure 1 Flow Chart of the Study Participants

Table 1 Characteristics of Participants who Completed the Study (n = 57)

Parameters	Intervention Group n = 29 (%)	Control Group n = 28 (%)	P-value
Maternal Factors at Baseline			
Weight Gain during Pregnancy (kg)	12.28 ± 3.54	13.82 ± 4.06	0.131
Duration of Sun Exposure (min/ day)	96.38 ± 68.44	98.57 ± 68.62	0.904
Sun Exposure per Day			0.760
≤ 15 min	5 (17.2)	4 (14.3)	
> 15 min	24 (82.8)	24 (85.7)	
Skin Color			0.109
Light Brown	5 (17.2)	1 (3.6)	
Medium Brown	19 (65.6)	17 (60.7)	
Dark Brown	5 (17.2)	10 (35.7)	
Sunscreen Use	9 (31.0)	6 (21.4)	0.410
Vitamin D Rich Food Consumption	5 (17.2)	1 (3.6)	0.194
Vitamin D Supplement	0 (0)	0 (0)	NA
Smoking	8 (27.6)	12 (42.9)	0.227
Pregnancy Complications	2 (6.9)	2 (7.1)	1.000
Serum 25(OH)D (ng/mL)	19.80 ± 8.96	19.41 ± 7.77	0.861
Vitamin D Sufficiency	2 (6.9)	1 (3.6)	1.000
Infant Factors at Baseline			
Gestation Age (week)	39.10 ± 0.95	38.89 ± 0.82	0.375
Birth Weight (g)	3126.03 ± 382.51	3063.57 ± 266.69	0.479
Length (cm)	50.62 ± 1.40	50.89 ± 1.37	0.461
Gender			0.689
Male	14 (48.3)	15 (53.6)	
Female	15 (51.7)	13 (46.4)	
Skin Color			0.130
Light Brown	8 (27.6)	3 (10.7)	
Medium Brown	20 (69.0)	21 (75.0)	
Dark Brown	1 (3.4)	4 (14.3)	
Type of Feeding			0.900
Breast Milk	19 (65.6)	18 (64.3)	
Infant Formula	5 (17.2)	4 (14.3)	
Mixed Feeding	5 (17.2)	6 (21.4)	
Season of Birth			0.612
Rainy	9 (31.0)	7 (25.0)	
Winter	20 (69.0)	21 (75.0)	
Serum 25(OH)D (ng/mL)	17.49 ± 4.34	18.69 ± 5.95	0.389
Infant Factors at 6 Months			
Duration of Sun Exposure (min/ day)	14.00 ± 15.97	15.82 ± 18.10	0.688

Table 1 Characteristics of Participants who Completed the Study (n = 57) (cont.)

Parameters	Intervention Group n = 29 (%)	Control Group n = 28 (%)	P-value
Sun Exposure per Day			0.681
≤ 15 min	14 (48.3)	12 (42.9)	
> 15 min	15 (51.7)	16 (57.1)	
Type of Feeding			0.063
Breast Milk	7 (24.1)	15 (53.6)	
Infant Formula	18 (62.1)	10 (35.7)	
Mixed Feeding	4 (13.8)	3 (10.7)	
Complementary Feeding			0.706
Yes	24 (82.8)	25 (89.3)	
No	5 (17.2)	3 (10.7)	
Weight (g)	7597.59 ± 852.77	7669.29 ± 775.02	0.741
Length (cm)	67.90 ± 2.26	67.61 ± 2.10	0.618
Serum 25(OH)D (ng/mL)	39.80 ± 12.69	35.79 ± 11.91	0.224
Serum Calcium (mg/dL)	10.34 ± 0.27	10.43 ± 0.32	0.310
Serum Phosphorus (mg/dL)	5.69 ± 0.42	5.64 ± 0.49	0.677
Alkaline Phosphatase (IU/L)	264.07 ± 77.65	281.00 ± 52.94	0.342
Serum iPTH (pg/mL)	27.96 ± 11.03	25.06 ± 8.58	0.275

Abbreviations: (OH)D, hydroxyvitamin D; cm, centimeter; dL, deciliter; g, gram; iPTH, intact parathyroid hormone; IU, international units; kg, kilogram; L, liter; mg, milligrams; mL, milliliter; n, number; NA, not applicable; ng, nanograms; pg, picograms

Data are presented as n (%) or mean ± standard variation, significant level at $p < 0.05$

Table 2 Effect of Vitamin D Supplementation on the Prevalence of Vitamin D Sufficiency and Mean Serum 25(OH)D of Infants at Six Months

	Intervention Group (n = 29)			Control Group (n = 28)			Multivariable Analysis ^c	
	At Baseline	At 6 Months	P-value ^a	At Baseline	At 6 Months	P-value ^a	Adjusted Change from Baseline between Two Groups	P-value ^b
Infants with Vitamin D Sufficiency (%)	8 (27.6)	28 (96.5)	0.002	11 (39.3)	23 (82.1)	0.044	1.76 (0.56 to 5.48)	0.331
Serum 25(OH)D (ng/mL)	17.49 ± 4.34	39.80 ± 12.69	< 0.001	18.69 ± 5.95	35.79 ± 11.91	< 0.001	7.07 (1.30 to 12.83)	0.016

Abbreviations: (OH)D, hydroxyvitamin D; mL, milliliter; n, number; ng, nanograms

Prevalence of vitamin D sufficiency was shown as frequency (percentage) and serum 25(OH)D as mean ± standard deviation, significant level at $p < 0.05$.

^a Multilevel Poisson regression with random intercept and fixed effect models was used to analyze the effectiveness of vitamin D supplementation on vitamin D sufficiency at 6 months compared to their baseline both intervention and control groups.

^b Multilevel linear regression with random intercept and fixed effect models was used to analyze mean difference in serum 25(OH)D from baseline to 6 months both groups.

^c Multilevel Poisson regression with random intercept and fixed effect models was used to analyze the effectiveness of vitamin D supplementation on vitamin D sufficiency over time (slope) by compared prevalence ratio of intervention group and control group.

^d Multivariable analysis adjusted for potential confounders including maternal factors (sun exposure, sunscreen used, vitamin D rich food consumption and vitamin D status) and infant factors (sun exposure, skin color, type of feeding and complementary feeding).

prevalence was higher in the intervention group than in the control group (96.5% vs. 82.1%), the difference was not statistically significant ($p = 0.331$). In both the intervention and control groups, the mean serum 25(OH)D levels of infants at 6 months of age was significantly higher than baseline levels ($p < 0.001$). After adjustment for potential confounders through multivariate analysis, the intervention group exhibited a mean increase of 22.30 ng/mL over baseline (95% confidence interval (CI), 17.98–26.62) in serum 25(OH)D levels at 6 months, which was 7.07 ng/mL (95% CI, 1.30–12.83 ng/mL) higher than that of the control group ($p = 0.016$).

To compare the effects of vitamin D supplementation on vitamin D status at 6 months of age among breastfed infants with those among formula-fed or mixed-fed infants (Table 3). At baseline, there were no significant differences in maternal or infant vitamin D status, nor in serum 25(OH)D levels between the intervention and

control groups across both feeding cohorts. Among breastfed infants, vitamin D supplementation resulted in significantly better outcomes at six months. Specifically, 100% of infants in the vitamin D group achieved vitamin D sufficiency, compared to 77.8% in the control group ($p = 0.046$). Furthermore, supplemented breastfed infants exhibited significantly higher mean serum 25(OH)D levels at six months ($p = 0.019$) and a greater increase from baseline ($p = 0.010$) relative to the control group. In contrast, these effects of vitamin D supplementation were not observed in formula-fed or mixed-fed infants.

DISCUSSION

In this study, vitamin D insufficiency or deficiency was observed in 66.7% of full-term newborns, which was similar to the high prevalence of these conditions among Thai neonates.³ Supplementation of vitamin D 400 IU/day significantly increased the prevalence of vitamin D

Table 3 Effect of Vitamin D Supplementation on Vitamin D Status of Breastfed Infants Compared to Formula-Fed or Mixed-Fed Infants

	Breastfed Infants			Formula-Fed or Mixed-Fed Infants		
	Intervention Group n = 19 (%)	Control Group n = 18 (%)	P-value	Intervention Group n = 10 (%)	Control Group n = 10 (%)	P-value
Maternal Data						
Vitamin D Status			1.000			NA
Deficiency or Insufficiency	17 (89.5)	17 (94.4)		10 (100.0)	10 (100.0)	
Sufficiency	2 (10.5)	1 (5.6)		0 (0)	0 (0)	
Serum 25(OH)D (ng/mL)	20.08 ± 10.54	19.85 ± 7.75	0.940	19.26 ± 5.22	18.61 ± 8.17	0.834
Infant Data at Baseline						
Vitamin D Status			0.743			0.582
Deficiency or Insufficiency	12 (63.2)	10 (55.6)		9 (90.0)	7 (70.0)	
Sufficiency	7 (36.8)	8 (44.4)		1 (10.0)	3 (30.0)	
Serum 25(OH)D (ng/mL)	18.18 ± 4.74	19.08 ± 6.14	0.620	16.18 ± 3.27	17.99 ± 5.85	0.405
Infant Data at 6 Months						
Vitamin D Status			0.046			1.000
Deficiency or Insufficiency	0 (0)	4 (22.2)		1 (10.0)	1 (10.0)	
Sufficiency	19 (100.0)	14 (77.8)		9 (90.0)	9 (90.0)	
Infant Serum 25(OH)D (ng/mL)	42.41 ± 13.02	32.57 ±11.14	0.019	34.84 ± 10.95	41.60 ± 11.55	0.196
Increment of Infant Serum 25 (OH) D from Baseline (ng/mL)	24.22 ± 12.76	13.59 ± 10.83	0.010	18.66 ± 10.94	23.61 ± 11.37	0.335

Abbreviations: (OH)D, hydroxyvitamin D; mL, milliliter; n, number; NA, not applicable; ng, nanograms

Data are presented as n (%) or mean ± standard variation, significant level at $p < 0.05$.

sufficiency and improved serum vitamin D levels among breastfed infants aged 6 months but not among formula-fed or mixed-fed infants. These findings are consistent with those of a previous study of Thai full-term breastfed infants, in which the mean serum 25(OH)D level was 46.01 ± 16.42 ng/mL and vitamin D sufficiency was present in 93.0% of infants aged 6 months who received vitamin D supplementation.¹⁷ According to our findings, daily supplementation with 400 IU of vitamin D significantly increased serum 25(OH)D levels by an average of 22.30 ng/mL over baseline (95% CI, 17.98–26.62). This mean increase is similar to that observed by Lin et al. in Taiwan (19.9 ng/mL; 95% CI, 18.7–38.6)²² but greater than those reported in a Cochrane review of nine studies involving 743 full-term breastfed infants (9.1 ng/mL; 95% CI, 6.8–11.3)⁶ and in a systematic review and meta-analysis of 25 studies of breastfed and formula-fed infants (13.9 ng/mL; 95% CI, 9.8–18.0).²³ These results suggest that vitamin D supplementation 400 IU/day, beginning in early infancy is effective for achieving serum 25(OH)D levels of > 20 ng/mL. Nearly all infants (96.5%) in our intervention group attained vitamin D sufficiency at 6 months, which confirms the effectiveness of supplementation in improving vitamin D status in healthy full-term infants. Of importance is that no infants in the intervention group exhibited clinical signs of vitamin D toxicity or had serum 25(OH)D levels exceeding 100 ng/mL throughout the study period; thus, the dosage of 400 IU/day was safe and effective, as in previous studies.^{7,10,17,19}

The mean serum 25(OH)D levels of infants at age 6 months were higher than those at baseline; thus, the prevalence of vitamin D insufficiency or deficiency among infants at age 6 months was reduced. These findings are consistent with those of previous studies.^{24,25} Oktaria et al. reported that the prevalence of vitamin D insufficiency or deficiency among Indonesian infants decreased from 90% at birth to 13% at 6 months.²⁴ Similarly, study of Nakano et al. revealed that serum 25(OH)D levels were higher in infants aged 6–15 months, even without supplementation, than in those aged 0–5 months, which indicates that vitamin D deficiency did not persist throughout infancy.²⁵ This increase in vitamin D levels in older infants may be attributed to higher dietary vitamin D intake after weaning and to greater sun exposure. However, our findings emphasize that vitamin D supplementation effectively increased serum vitamin D levels and the

prevalence of vitamin D sufficiency among breastfed infants at 6 months of age, whereas no such effect was observed in formula-fed or mixed-fed infants. Breast milk contains vitamin D at concentrations ranging from 15 to 50 IU/L, significantly lower than the levels found in infant formula (400 IU/L). Consequently, breastfed infants are at a higher risk of vitamin D deficiency, and supplementation is thus particularly beneficial for this group. Furthermore, the relatively high vitamin D levels observed in the control groups at 6 months of age raise the possibility that routine vitamin D supplementation beyond this age may not be necessary; however, this finding should be interpreted with caution and warrants further investigation.

A daily intake of 400 IU of vitamin D is sufficient to prevent rickets in children and is recommended for all infants from birth to 12 months of age, regardless of feeding method.^{14–16} Current evidence supporting the recommendation of vitamin D supplementation to prevent deficiency in Asian infants has been increasing.^{26,27} These guidelines typically advise vitamin D supplementation without prior screening, as the cost of blood testing is considerably higher than that of supplementation.^{14–16,26,27} Despite these recommendations, vitamin D supplementation for healthy full-term infants is not widely practiced in Thailand, possibly because of the absence of national guidelines and the limited availability of studies focusing on Thai infants.¹⁷ This study underscores the benefits of vitamin D supplementation in restoring adequate vitamin D status in full-term breastfed infants.

This study demonstrates a high prevalence of vitamin D deficiency or insufficiency among mothers. Because maternal vitamin D status determines the vitamin D content of breast milk, maternal deficiency may result in inadequate vitamin D intake in exclusively breastfed infants, particularly without supplementation.^{28,29} Current guidelines recommend adequate vitamin D intake during pregnancy and lactation to support maternal and neonatal vitamin D status.³⁰ Our findings highlight the potential benefit of optimizing maternal vitamin D status during pregnancy and breastfeeding to improve infant vitamin D status. Further research is needed to assess the combined effects of maternal and infant vitamin D supplementation

This study had several strengths. To the best of our knowledge, this is the first double-blind, randomized, placebo-controlled evaluation of the effect of vitamin D supplementation on the vitamin D status of healthy full-term Thai infants. While a previous randomized

controlled trial in Thai infants has been reported,¹⁷ that study employed an open-label design despite its larger sample size. The double-blind, placebo-controlled design of the present study minimizes potential bias and strengthens the internal validity of the findings. Baseline characteristics and serum 25(OH)D levels of both infants and their mothers were assessed and confirmed comparability between the intervention and control groups at study entry. In addition, by including both breastfed and formula-fed infants, the findings may be generalizable to a broader infant population.

This study has several limitations. It was conducted at a single hospital with a modest sample size, which may limit generalizability. Lifestyle factors influencing vitamin D status were not comprehensively assessed, potentially introducing recall bias, and the short follow-up limited evaluation of long-term outcomes. Additionally, intention-to-treat (ITT) analysis was not feasible because participants lost to follow-up had no post-baseline serum 25(OH)D data. Given the modest sample size, advanced methods for handling missing data would rely on unverifiable assumptions and could introduce bias. Therefore, the findings should be interpreted cautiously, particularly regarding internal validity.

Future multicenter studies with larger samples and longer follow-up are warranted to enhance generalizability and permit both ITT and per-protocol analyses, thereby providing more robust estimates to inform national vitamin D supplementation guidelines.

CONCLUSION

This study highlighted the high prevalence of vitamin D insufficiency and deficiency among healthy Thai neonates. Daily supplementation with 400 IU of vitamin D from birth to 6 months of age significantly improved the prevalence of vitamin D sufficiency and elevated serum vitamin D levels at age 6 months among the breastfed infants without any adverse effects. However, these benefits were not observed in formula-fed or mixed-fed infants.

Conflict of Interest

The authors declare no conflict of interest.

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Formal analysis: T.T., S.T.

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Investigation: T.T., S.T., R.P.

Methodology: T.T., S.T.

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Resources: S.T., R.P.

Software: T.T.

Supervision: S.T.

Validation: T.T., S.T.

Visualization: T.T.

Writing – original draft preparation: T.T.

Writing – review & editing: S.T., R.P.

Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on request.

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REVIEW ARTICLE

Capitation Payment Schemes for Primary Health Care in Low- and Middle-Income Countries: A Scoping Review

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ABSTRACT

Objectives: This study aimed to examine the implementation and evaluation of capitation payment schemes in primary health care (PHC) across low- and middle-income countries (LMICs). In particular, it focused on how these schemes are being implemented in real-world settings where data in LMICs are limited. The study also aimed to identify challenges in implementation and assess the contextual factors that influence the sustainability of capitation-based health financing strategies.

Materials and Methods: A scoping review was conducted using the PRISMA extension for scoping reviews (PRISMA-ScR) framework to systematically gather and synthesize the existing literature in the Sustainable Development Goals period published between 2015 and 2024. A comprehensive search was carried out in PubMed, OvidSP, and Scopus using strategic keywords related to capitation payments, PHC, and LMICs. After 456 initial records were scrutinized, 40 full-text articles were included. The literature were evaluated for implementation attributes, effectiveness, contextual challenges, and policy characteristics. Data extraction and analysis followed the Population, Concept, Context framework and were validated by an independent evaluator.

Results: This research identified 12 LMICs across four continents that have adopted capitation payment schemes for PHC. A wide range of implementation strategies was observed, depending on the context of each country. Significant challenges were identified in data reliability, politically, budget allocation, and policy planning. Evidence gaps were particularly evident in low-income countries, particularly during the pre-implementation phase of policy design, and the lack of diverse outcome evaluations or policy assessments.

Conclusion: Capitation payment schemes present promising opportunities to strengthen PHC and advance universal health coverage goals in LMICs. However, their success is highly dependent on local political, economic, and institutional contexts. Tailored implementation strategies, robust monitoring systems, and improved pre-implementation planning are essential to enhance policy effectiveness and sustainability. Future research should focus on standardized evaluation frameworks throughout the implementation process and on distinguishing policy effects from implementation fidelity.

Keywords: capitation payment, LMICs, essential health services, national healthcare system, primary healthcare

INTRODUCTION

Primary health care (PHC) is a whole-of-society approach that delivers accessible, comprehensive, continuous, and person-centered health services, integrating prevention, promotion, treatment, rehabilitation, and palliative care, while addressing the broader determinants of health. PHC serves as the foundation for achieving universal health coverage (UHC), which is a core component of the Sustainable Development Goals (SDGs) agenda. There is substantial evidence that PHC interventions are cost-effective in low- and middle-income countries (LMICs).^{1,2} The PHC sector in the health care system has a profound influence on the interactions and relationships between government, providers, purchasers, and the population across the entire health care landscape. Providers' payments play a key role in pushing broader health systems to gain financial control and overcome financial incentives to fund PHC.³ Current mechanisms for mobilizing and pooling health funds in LMICs suffer from several weaknesses due to fragmented and inadequate revenue sources, as well as inherent challenges in sharing and managing resources.⁴ Payment models for PHC providers can create financial incentives that have a profound effect on provider behavior, patient care, and health system efficiency.⁵ These models include input-based, service-based, performance-based, and population-based payments, with each option potentially providing specific incentives.³ Therefore, capitation payment schemes, particularly in PHC, have increasingly focused on different payment mechanisms to finance UHC targets in LMICs.

The LANCET Global Health Committee on Financing PHC stated, "The Commission's vision for PHC provider payment is a context-specific blended payment model built on capitation."⁶ The capitation payment transfers the financial risk from the buyer to the provider, separating the provider's payment from the volume of services delivered. Providers are responsible for any costs that exceed their preset capitation budget, whereas any savings can be retained and reinvested. This structure incentivizes providers to increase efficiency, attract more patients, and focus on improving the quality of care.³ Although capitation payment programs theoretically address known financial inadequacies, the contexts and issues in PHC differ across LMICs. Despite its critical importance, PHC in LMICs continues to face significant challenges in policy implementation, and there is limited literature focusing on this topic.⁶ Existing research findings

reported that the provider payment reform (PPR) system should improve hospitals' management capabilities by taking into account both PPR and reimbursable and non-reimbursable expenses.^{7,8} Other research reports that capitation in PHC deviates from economic and tax principles. Studying global PHC perspectives and reimbursement information could lead to the establishment of new standards for reporting in PHC systems.^{9,10} For example, some studies also indicated that LMIC financing reforms on reimbursement are well-functioning primarily during the COVID-19 pandemic, and PHCs are the best platform for providing basic healthcare services.^{11,12} PHC in LMICs continues to face significant challenges in policy implementation, and the literature on this topic remains limited.⁶ For instance, existing multinational reviews are often skewed toward high-income countries because the evidence base is more extensive, whereas reviews that focus on LMICs frequently examine policy effects within only one LMIC setting.^{13,14} Therefore, this study is the first scoping review to map and synthesize evidence on PHC capitation across multiple LMICs. We focus on how capitation in PHC is being implemented and what the results are. The findings of this study will help identify more effective and sustainable health financing strategies to support the achievement of UHC and improve health outcomes in LMICs.

MATERIALS AND METHODS

We conducted the scoping review using the Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).¹⁵ PRISMA-ScR compiled evidence from the academic literature on capitation payment schemes and informed decision-making on sustainable health financing strategies to support UHC goals and improve health outcomes in LMICs.^{6,15} PRISMA-ScR addresses the lack of available literature on capitation payments as well as research gaps on the implementation of capitation payments in PHC in LMICs.^{15,16} The two evaluators (DM and TC) have verified the accuracy of the data processing, analysis, presentation, and validation. The scoping review eligibility criteria are i) geography: low-to-middle-income countries; ii) study focus: capitation payments alone, or combined with other payment methods within the PHC schemes; iii) study design: any analytical or observational study, and any research method, quantitative, qualitative, or review (no primary data); iv) language: English; v) publication type: peer-

reviewed journal, and grey literature; and vi) publication period SDGs era from 1 January 2015 to 31 October 2024.

First, we conducted a scoping review of the search criteria. The preliminary search was performed in PubMed, the well-known medical database, to identify and examine a study topic.¹⁷ This step defines the appropriate search criteria before developing a search strategy and finalizing the search criteria. Thus, the preliminary results revealed that the terms “LMIC” and “developing country” did not yield any results in the primary focus of this study. Importantly, the search terms “LMIC” and “developing country” were defined prominently by the World Bank and the United States National Library of Medicine’s Medical Subject Headings database, respectively.^{18,19} Consequently, we manually searched for these search terms in PubMed, OvidSP, and Scopus to identify the foci of the studies in the titles and abstracts.^{17,20,21} Hence, we then retrieved full-text articles published in English from 2015 to 2024 during the SDGs period for analysis.²² Multilingual translation is excluded because current AI-powered translation systems (such as Google Translate) have capabilities that are more limited than those of humans.²³ **Table 1** shows strategic keywords in the search, and the search strategies were not limited to medical subject headings (MeSH) terms alone. The authors conducted cross-checks through plain-text search using keywords from research concepts such as PHC, capitation, and LMICs (**Table 1**). After the initial scoping search, we removed the MeSH term and plain-text keywords for “LMIC” and “developing

countries” because they did not reliably retrieve all relevant studies.

We tabulated the results of the literature search in EndNote 21 (Clarivate Plc, Philadelphia, PA, USA). We removed duplicated literature titles and then saved the .enl file format for further analysis. Titles and abstracts were screened and assessed based on the search strategy. The independent evaluators (DM and TC) then scrutinized the full texts of the articles. The independent observers (DM and TC) analyzed and verified that the data from the literature were in line with the capitation payment, PHC, and LMIC included in this scoping review.

Two independent evaluators (DM and TC) extracted the following verified data from the literature as follows: country, first author, year of publication, type of capitation payment, implementation scale, PHC quality, study context, and affected area. The data extractions were then standardized to transform the synthetic data into consistent data and generate the presentation data according to the study description and study topic focus.¹⁵ The LMICs data patterns for the number of publications were extracted and presented in this scoping review.²⁴ We analyzed the research methodologies used in the verified literature data into four categories: review, quantitative, qualitative, and mixed methods (categories 1 to 3). The capitation payment challenges and facilitators were characterized into four periods: exploration, adoption decision or preparation, active implementation, and sustainability.

The independent evaluators and observers (DM and TC) ensured that this scoping review complied

Table 1 The Search Keywords

Databases	Operational Search Keywords
PubMed	(“capitation fee”[MeSH Terms] AND (“primary health care”[MeSH Terms] OR (“primary”[All Fields] AND “health”[All Fields] AND “care”[All Fields]) OR “primary health care”[All Fields] OR (“primary”[All Fields] AND “care”[All Fields]) OR “primary care”[All Fields])) AND (English [Language]) AND 2015/01/01:2024/12/31[Date - Publication]
OvidSP	((“capitation .mp”) AND (“primary care.mp” OR “primary health care.mp” OR “community care.mp” OR “general practitioner.mp” OR “family medicine.mp”)) AND (“limit to english language”) AND (“yr=”2015-Current”))
Scopus	TITLE-ABS (“capitation”) AND TITLE-ABS (“primary care” OR “primary healthcare” OR “primary health care” OR “general practitioner” OR “community care” OR “family medicine”) AND PUBYEAR > 2015 AND PUBYEAR < 2024 AND (LIMIT-TO (LANGUAGE , “English”))

Abbreviation: ABS, abstract

with the guidelines published by the Joanna Briggs Institute.²⁵ The focus of this study was developed based on the Population, Concept, and Context principles to ensure that data were analyzed and presented in a manner that provided clarity and meaningful titles for the scoping review.²⁶ This review's primary objective was to effectively address the research questions of the studies, which involved the direct extraction of data to answer the study's focused question. The bias-minimization steps included ensuring that the research objectives were met, the research questions were answered, and the evaluation and results were fair.²⁷ All processes in the scoping review were first

verified and confirmed by the first verifier (DM), and then by the second verifier (TC). Hence, the results presented in this study can be reproduced for data processing.

RESULTS

Figure 1 shows a flowchart of the final scoping review using PRISMA-ScR. The literature search yielded 456 publications. After we removed the duplicates, 259 publications remained. We screened a total of 259 titles and abstracts and identified 191 publications as mismatching the study criteria. Subsequently, 68 full-text publications were scrutinized, and 28 studies

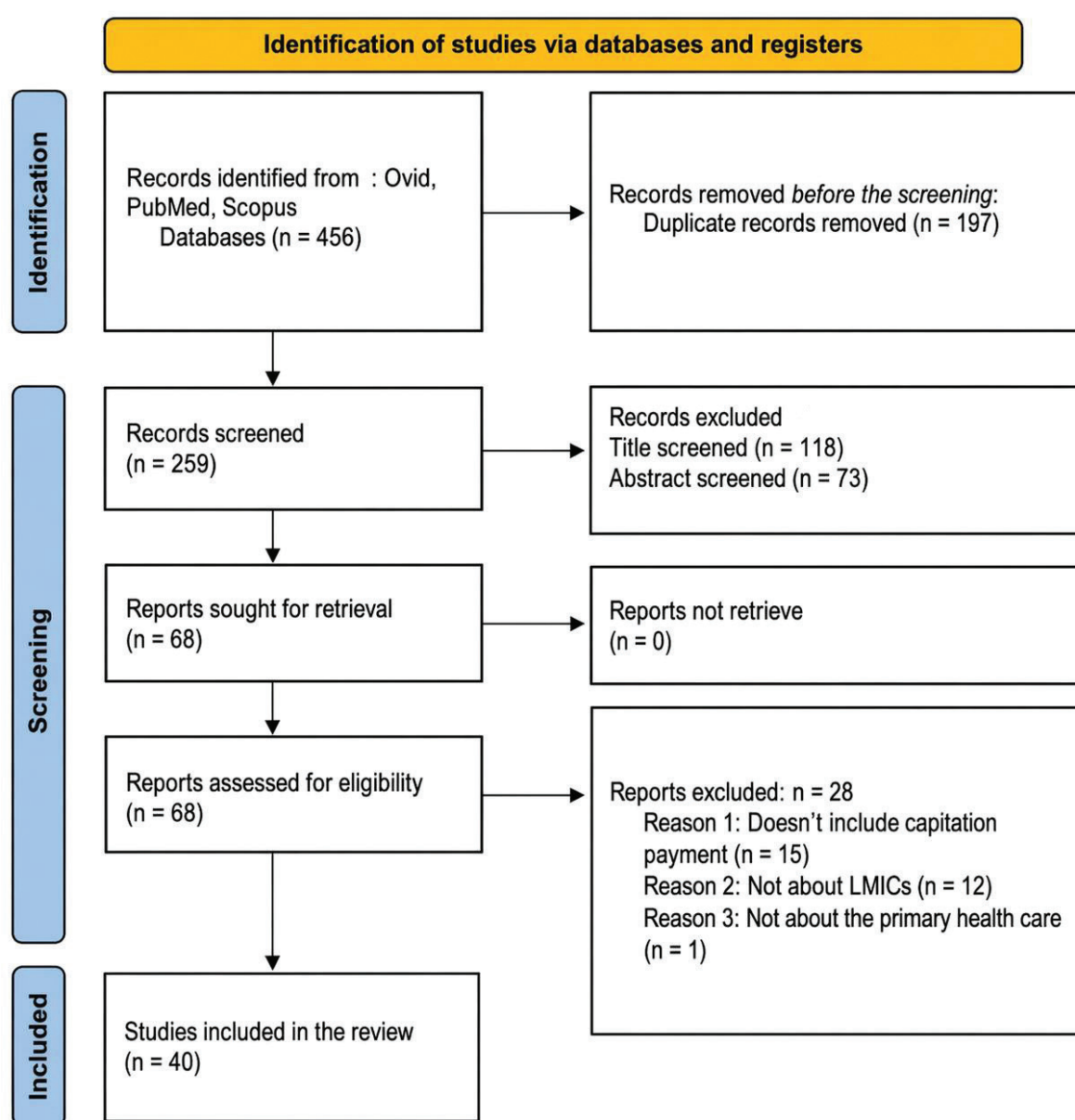


Figure 1 Algorithm Search for Scoping Review

were removed because they did not meet the focus of the study. Consequently, this scoping review comprised 40 full-text articles, as shown in **Figure 2**.

Of the 40 articles, 12 LMICs implemented capitation payment schemes for PHC across four continents: Asia, Europe, South America, and Africa. First, six countries on the Asia continent consisted of Southeast Asia (Indonesia), South Asia (India), East Asia (China and Mongolia), West Asia (Iran), and Central Asia (Tajikistan). Second, the three countries on the African continent are Ghana, Kenya, and Tanzania. Third, two countries were in Eastern Europe:

Georgia and Ukraine. Finally, one country in South America (Brazil) was included.

An evaluation of capitation payments in PHC is divided into eight attributes: (1) Adoption, (2) Acceptability, (3) Cost, (4) Effectiveness, (5) Feasibility, (6) Reach, (7) Sustainability, and (8) Chance. **Table 2** depicts the evidence of the study contexts. **Table 3** summarizes the 12 LMICs across four continents and characteristics of the studies included in this scoping review, revealing shared knowledge on capitation payments.

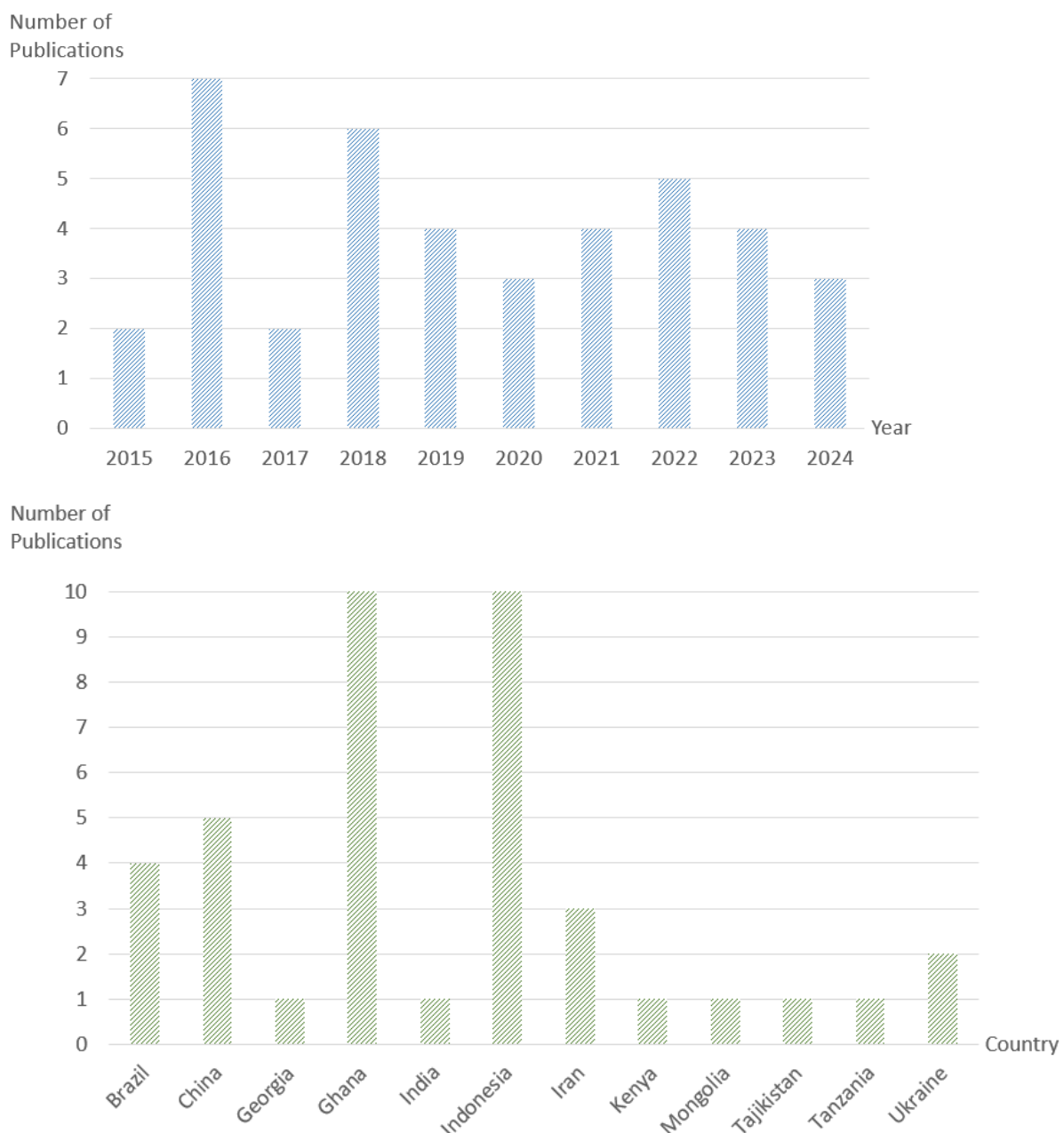


Figure 2 Capitation Payment Literature Results from LMICs (matched to Tables 3 and 4)

Table 2 Attributes for Evaluation of Capitation Payment Assessment in PHC

Attributes	Contexts
1- Adopt	Policies are promulgated at the regional or national levels. The regional policies are being implemented.
2- AB	Patients' perception of the policy and stakeholders' perception of the policy.
3- CST	Monetary and non-monetary resources for operations and implementations.
4- EFF	Primary care cost, primary care service utilization, and primary care quality assessments.
5- FS	Operation and deployment can overcome the challenges of capitation payment and support facilitators.
6- Reach	Characteristics of individuals affected by the facts of policy are detailed.
7- Sustain	Implementation outcomes over time.
8- CHC	Adverse effects such as increased drug costs and characteristic changes in healthcare personnel.

Abbreviations: AB, acceptability; Adopt, adoption; CHC, chance; CST, cost; EFF, effectiveness; FS, feasibility; Sustain, sustainability

Table 3 A Characteristic of Scoping Review Literature

Continent	Country		Capitation Payment Assessment							
			1	2	3	4	5	6	7	8
			Adopt	AB	CST	EFF	FS	Reach	Sustain	CHC
Asia	Southeast	Indonesia	✓	✓	✓	✓	✓	✓	✓	✓
	South	India								
	East	China	✓		✓	✓		✓	✓	
		Mongolia	✓					✓	✓	
	West	Iran	✓	✓	✓	✓	✓	✓		
	Central	Tajikistan	✓							
	West Coast	Ghana	✓	✓	✓	✓	✓	✓	✓	
African	East Coast	Kenya	✓		✓	✓		✓		
		Tanzania	✓	✓	✓					
		Georgia								
Europe	Eastern	Ukraine	✓	✓	✓		✓	✓	✓	
		Brazil	✓		✓	✓		✓	✓	
South America	Eastern									

Abbreviations: AB, acceptability; Adopt, adoption; CHC, chance; CST, cost; EFF, effectiveness; FS, feasibility; Sustain, sustainability

Table 4 illustrates the evidence of the capitation payment schemes found in this scoping review. We examined the implementation policies in each nation's strategies for implementing capitation policies, considering whether capitation payment was integrated into national PHC models or reforms. A primary reason for

selecting a specific region for implementation in each country was to enable policy implementation and assess its effects before nationwide implementation.

In addition, we categorized the effectiveness of the capitation payments in PHC into three categories: cost-effectiveness, utilization, and quality (**Table 5**).

Table 4 Capitation Payment Schemes

Year	Country	Reach		Policy	Strategy	Capitation Type
		Region	Level			
2019	Brazil	All	Nationwide	Prevent Brazil	PHC reform	Weighted capitation, performance-based payment, and incentives for strategic actions ^{28,29,30-31}
2017	Ukraine	All	Nationwide	Government financial guarantees of healthcare services	National health financing reform	Weighted capitation ³²⁻³³
2017	Tanzania	All	Nationwide	Direct health facility financing of health basket funds	New provider payment method	Weighted capitation ³⁴
2015	Kenya	All	Nationwide	NHIF outpatient capitation under the Supa cover	PHC financing schemes	Capitation payment ³⁵
2014	Indonesia	Padang, Pekanbaru, and Jambi	District to Nationwide	National health insurance initiatives	PHC reform	Weighted capitation with performance pay ³⁶⁻⁴⁵
2011	China	Shanghai	District to Nationwide	National health reform of the new rural cooperative medical schemes	Healthcare reform	Capitation payment ⁴⁶⁻⁴⁹
		Ningxia	District to Nationwide	Ningxia project	Healthcare reform	Capitation payment with performance pay ⁵⁰
2011	Iran	Tabriz	District	Urban family physicians project	n/a	Weighted capitation with performance pay ⁵¹⁻⁵³
2011	Mongolia	All	Nationwide	n/a	National health act on PHC	Weighted capitation ⁵⁴
2010	Ghana	Ashanti	District	National health insurance schemes	Capitation pilot	Capitation payment ⁵⁵⁻⁶⁴
2010	Tajikistan	Dangara and Varzob	District	n/a	Pilot project on capitation-based financing for PHC	Partial capitation ⁶⁵
n/a	Georgia	n/a	n/a	n/a	PHC reform	Capitation payment ⁶⁶
n/a	India	n/a	n/a	n/a	Scale-up PHC	Weighted capitation ⁶⁷

Abbreviations: n/a, not applicable; NHIF, The national health insurance fund; PHC, primary health care

Cost-effectiveness measures the expenditure costs of PHC after the implementation of the capitation payment policy. Utilization measures the number of patients using PHC services, whereas quality measures different forms of PHC by analyzing the quality of medical personnel or services provided by PHC. Overall, measures of cost-effectiveness suggest that the policy is largely associated with reduced costs. Utilization measures indicate an overall increase, consistent with improved healthcare access and service use. Findings on quality of care are mixed, likely reflecting heterogeneity in study designs, outcome definitions, and analytic methods across the included research.

Based on the implementation steps and context adapted from the conceptual model, we categorized the challenges into four stages: exploration, decision/implementation preparation, implementation, and maintenance. The evidence from the scoping review showed that the post-implementation phase, facilitator

area, and process evaluation posed significant challenges in implementing capitation payments in PHCs. Hence, it is assumed that countries that can overcome these challenges will develop a more resilient PHC and a stronger UHC for their citizens. **Table 6** reveals the challenges in implementing capitation payments in the PHC.

DISCUSSION

Capitation payment management for PHC in LMICs remains limited to well-known international digital health databases (**Figure 2**) (**Table 2**). The main reason is that LMICs that have implemented capitation payment systems often do not disclose knowledge management in international health databases. In addition, some countries may publish knowledge on capitation payment management in their local journals and in languages other than English. For example, low-income countries (LICs) such as Ethiopia have

Table 5 Capitation Payment Evaluation

PHC	Mixed-Methods		Quantitative		Qualitative	
	Measures	yr	Outcomes	Measures	yr	Outcomes
Cost-effectiveness	Budget post implementation	2	Increased by 8% ²⁸	Outpatient cost	4	Increased by 6% ⁴⁷
	Total medical expenditure	1	Decreased by 4% ⁴⁶	Inpatient cost	4	Increased by 35% ⁴⁷
	Total expenditure of funds	1	Decreased by 4% ⁴⁶	OOP payments	2	10% higher probability of OOP ⁵⁵
	Average expenditure per outpatient visit	1	Decreased after the 3 rd month ⁴⁶			
	Average expenditure per hospital stay	1	Increased by 14% ⁴⁶	Income and expenditure of the National Health Insurance scheme	4	Expenditure exceeds the income after 2 years. ⁵⁶
	Ratio of OOP payment medical expenses to annual net income per capitation	1	Increased by 0.5% ⁴⁶			
Utilization	Outpatient's utilization	2	Increased by 2% ⁴⁶	Registration population	2	Increased by 56% ²⁹
	Outpatient visits per capitation	2	Increased by 16% ⁴⁶	Capitation of outpatient visits	4	Increased from 14 times to 20 times ⁴⁷
	Outpatient visits	2	Increase utilization in rural areas ⁴⁶	Use of outpatient care	1	Increased by 47% ⁵⁰
	Health services coverage	3	Increased, but no difference compared to the district without capitation. ³⁶	Contact rate	1	Positive contact rate ²⁶
				Access to PHC services	9	Influenced by awareness ³⁵
Quality	Oral health	1	Increased capital by 32%, and increased working hours. ²⁸	Medical seeking behavior (outpatient)	4	Increased tertiary care services by 10% ⁴⁷
				Medical seeking behavior (inpatient)	4	Increased tertiary care services by 3% ⁴⁷
				Quality score (first contact, continuity of care, coordination, comprehensiveness)	2	Scores were similar between the two districts. ⁴⁸ Increased significantly compared with the control group. ⁴⁹

Table 5 Capitation Payment Evaluation (cont.)

PHC	Mixed-Methods	Quantitative	Qualitative
PHC	Number of higher education health professionals	1 Increased by 16% ²⁸	2 Follow-up rates increased but did not differ between control groups. ⁴⁹
			2 Quality perception in the region (per capita rate) was lower compared to the control group. ⁵⁷
			2 No differences from the control group ⁵⁵
	Classification by quality	4 Maximize quality but make no difference compared to districts without capitation. ³⁶	4 Provisions of ANC4+ in hospitals ⁵⁸
			2 Increased by 1% of chronic patients compared to the control group. ³⁷
		Satisfaction	5 Satisfaction has increased over time, but not due to capitation reform. ⁵⁸

Abbreviations: ANC4+, antenatal care - ANC; n/a, not applicable; NCD, noncommunicable diseases; OOP, out-of-pocket; PHC, primary health care; yr, year: time after the implementation
 ANC4+ indicates the number of times a woman's health is checked during pregnancy using standard questions.²

Table 6 Challenges of Capitation Payment and Support Facilitators for PHCs

Post-Implementation Phase	Facilitator Area	Process Evaluation
Exploration	Fundings	Miscalculation of cost rates leads to a lack of funding. ⁵⁶
	Sociopolitics	Setting unrealistic targets ³⁶
		Setting upper and lower bounds upon the capitation results in gaming the system. ³⁶
		A team of experts supported by international and national institutions developed a new Brazilian PHC financing model by examining federal lending and analyzing best practices from national and international literature. ³⁰
Adoption decision or preparation	Interorganizational networks	Lack of communication between the regional and central governments ⁴³
	Sociopolitics	Implementers involved politicians, which created the impression that capitation policy was a political issue ⁵⁶
	Organizational characteristics	The patient's lack of trust in the implementers ^{56,59}
Active implementation and sustainment	Adopter characteristics	Patients' lack of trust in the health providers ⁶¹
		PHC funds management autonomy ⁴⁰
		Lack of knowledge of the policy ^{39,42}
		Unequal implementation readiness ³⁹
		Patient's behavioural issues led to requesting unnecessary medications and referrals. ⁵¹
	Fundings	Delay in reimbursement claims ⁵⁹
		Overbilling practices ⁵⁶
		Health promotion activities ³⁹
	Fidelity monitoring or support	Regulations were rewritten to be more user-friendly. ³⁹
		Active monitoring and enforcement of the rule by providers ⁴⁰
		Slow internet is hindering efficiency and regular monitoring. ⁴⁰
		Lack of onsite technical support and regular information systems ^{36,40}
	Public-academic collaborations	Ability and competency to conduct high-quality research ³⁹
	Sociopolitics	Stakeholders' perception towards capitation ^{56,64}
		Patient's perception towards capitation ^{56,62}
		Low enrolment rates ⁵⁹

Abbreviations: PHC, primary health care

implemented capitation payment systems for PHC but have not published documents on capitation payment management, nor have they published literature in international publications.⁶⁸ Another consideration is that, in some countries, capitation policies were implemented only at a subnational or regional level (Table 5). When these initiatives did not meet expectations, subsequent policy expansion and related research activity may have stalled, resulting in limited published evidence. Therefore, researchers should be encouraged to conduct and share their knowledge with other academics, especially in LICs and LMICs.

In addition, another important gap lies in pre-implementation studies of capitation payment management for PHC models or pilot projects. As a result, this limits our understanding of the preparatory steps required for implementation fidelity, such as exploring the sociopolitical context, funding mechanisms, and organizational readiness.^{69,70} Furthermore, excluding non-English publications might result in the omission of important information, especially in LIC countries. Therefore, we address this gap in this review by presenting evidence in Table 6 regarding how to overcome the challenges in capitation payments to achieve sustainable capitation payments for PHC.

Importantly, this scoping review identifies the key factors that influence implementation outcomes, including funding mechanisms, monitoring approaches, and the political and socioeconomic context. Challenges in budget formulation and implementation have a significant effect on the capitation plan. For instance, in Ghana, the capitation spending rates were based on erroneous data from previous payment systems, raising concerns about inadequate budget allocation.⁵⁶ In contrast, Brazil uses an equity-weighted payment criterion to address socioeconomic and demographic inequalities.³⁰

This review identified several factors that influence the implementation outcomes. For example, as a result of many factors, Indonesia has found success and continued to implement capitation payments for PHC.⁴¹ This country has also implemented an efficient budget, with strict monitoring and enforcement mechanisms, allowing PHC facilities to independently manage their funds and improve the quality of services. Table 5 shows the Indonesian capitation payment scheme. Implementation fidelity and transparent reporting are equally important, as seen in Indonesia,

where the ability to analyze accurate data supports policy maintenance and adaptation.³⁹ Political and socioeconomic factors also play an important role. Political alignment among stakeholders, leaders, technical experts, and activists can influence policy prioritization and legitimacy. For instance, in Ghana, a lack of prioritized budget allocation and problems of political legitimacy hinder successful implementation.⁵⁶ In summary, we found that implementation is shaped by multiple, context-specific factors that vary across countries, even in countries that employed a capitation policy nationally for several years. This heterogeneity complicates efforts to draw clear, generalizable conclusions about the determinants of successful implementation. Accordingly, our findings underscore the importance of tailoring capitation payment models to each setting's political, economic, and institutional context during design and rollout.

Another key point from this literature review analysis shows a variety of outcome measures for capitation payment policies, which complicates the efforts to draw clear conclusions. Financial assessments often focus on the total PHC costs or the patients' costs, the latter of which allows for a clearer understanding of equity implications.⁷¹ For example, service outcomes were measured on the outpatient visits and chronic disease management. These results are important in the assessment of health access and promotion but are often influenced by broader health reforms, which confound policy-specific effects. Alternatively, quality of care assessment is generally based on patient perceptions, examining dimensions such as continuity of care and comprehensiveness of services. Stakeholder perceptions gathered through interviews and surveys provided a deep understanding of the implementation challenges and areas for improvement.⁷² In addition, the measures of stakeholder perception in PHC. Moreover, the interrelated nature of capitation payments and broader reforms complicates that attribution of outcomes to a single payment model.⁷³ Addressing these issues requires standardized assessment measures that isolate the impact while considering contextual variables.

Future policymakers should ensure accuracy and guide policy changes; comprehensive data collection at every stage of the implementation is essential for strong monitoring. Developing a tool to map national PHC financial ecosystems could provide a foundation for informed policymaking.¹⁵ Financial assessment

should focus on equitable resource distribution and allocation within PHC facilities using advanced methods such as the health resource density index.⁷⁴ In addition, future research studies should distinguish between implementation outcomes and policy outcomes to clarify whether observed possessions are due to capitation payment models or their implementation. To capture the role of populations in shaping PHC systems, service evaluations should focus on patient-focused outcomes, such as preventive care utilization and provider selection, especially the equity aspect, such as access for the vulnerable population. The assessment of institutional structures, particularly the independence of service providers, requires a qualitative approach to contextualize decision-making processes and resource allocation challenges.⁴

For literature gap during reimplementation phase of the policy, we propose a simple implementation timeline to structure planning and reporting: (i) Pre-implementation, including readiness assessment, stakeholder engagement, and budget/enrolment modelling; (ii) Pilot phase, involving limited rollout with predefined indicators for cost, utilization, and quality; (iii) Scale-up, characterised by gradual expansion with iterative adaptation based on monitoring results; and (iv) Sustainability, requiring continuous monitoring, equity safeguards (e.g., risk/needs adjustment), and transparent reporting to maintain accountability and policy learning. These recommendations are intended to increase the rigor and relevance of future research methods and support evidence-based policy development.

In summary, four take-home messages emerge. First, capitation implementation is strongly context dependent, shaped by financing arrangements, political legitimacy, and institutional capacity. Second, strong monitoring and data systems (accurate enrolment/budget modelling, routine indicators, and transparent reporting) are critical to sustain and adapt reforms. Third, the equity effects of design choices (e.g., weighted vs flat-rate capitation) remain insufficiently evaluated to support firm conclusions. Finally, major research gaps persist, limited pre-implementation evidence, heterogeneous outcome measures, and sparse LIC data highlighted the need for prospective, standardized evaluations that document implementation fidelity and track cost, utilization, quality, and equity over time.

This scoping review provides a broad overview of capitation policy research in PHC, identifying key gaps in geographic coverage and methodology. It emphasizes the need for a more in-depth analysis of the implementation processes and contextual factors that influence policy outcomes in individual countries. This work relies on a single reviewer (DM) for reviewing and scrutinizing the limits of its methodological robustness. Unlike our previous systematic reviews, this method does not assess the quality of studies; instead, it provides generalized results rather than specific, actionable insights.^{75,76} The exclusion of non-English publications further narrows the scope, potentially omitting important contributions from non-English-speaking countries. Despite these limitations, this review provided valuable guidelines for future research, emphasizing the importance of addressing geographic differences, improving assessment measures, and integrating preimplementation studies into the evidence base. Therefore, researchers can better inform the development of equitable, effective, and sustainable capitation payment models for PHC in LMICs.

CONCLUSION

Overall, evidence shows that capitation payment in primary healthcare is frequently associated with reduced costs and increased utilization, while reported effects on quality of care are mixed and difficult to compare due to heterogeneous outcomes and methods. The review also identified substantial evidence gaps, particularly limited pre-implementation analysis, sparse reporting from LICs, and insufficient evaluation of equity-oriented design features (e.g., weighted versus flat-rate payments) and monitoring systems. In conclusion, capitation reforms for PHC should be supported by comprehensive, stage-specific data collection to strengthen monitoring, guide mid-course adjustments, and improve accountability. Policy and evaluation should incorporate an explicit equity lens, mapping the national PHC financing ecosystem and assessing resource distribution within facilities (e.g., using health resource density metrics). Future research should separate policy effects from implementation fidelity, use patient-centred and equity-sensitive outcomes, and address the pre-implementation evidence gap by reporting systematically across the stages of pre-implementation, pilot, scale-up, and sustainability.

Conflict of Interest

The authors declare no conflict of interest, no personal relationships, and no financial interests that have influenced the research reported in this paper.

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Author Contributions

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Data Availability Statement

The data are included in this article. Please do not hesitate to contact the authors or the corresponding authors for any enquiries regarding this study.

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