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The current situation of health services for hydatidiform mole in Cambodia

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Abstract

Aim: Management of hydatidiform mole is important to reduce the mortality and morbidity of choriocarcinoma. This study aims to understand the existing health services for hydatidiform mole and to estimate the incidence of gestational trophoblastic disease (GTD) in Cambodia.

Methods: A questionnaire was used to collect information on the existing health services for pregnancy and hydatidiform mole at health facilities from attendants of the 16th Annual Conference of the Cambodian Society of Gynecology and Obstetrics in 2017. The incidence of GTD in 2014–2017 was estimated using Health Information System data.

Results: A total of 126 attendants, who were from all provinces except three provinces, answered the questionnaire. The work places were national hospitals ($n = 29$), provincial hospitals ($n = 42$), district hospitals ($n = 20$), health centers ($n = 6$), and others ($n = 29$). The answers of participants from the public sector suggested the following: Ultrasonography is available at all hospitals but not health centers; Human chorionic gonadotropin (hCG) measurement is only available at national hospitals; Treatment of hydatidiform mole is performed at national hospitals and provincial hospitals; and Treatment of gestational trophoblastic neoplasia (GTN) is provided at national hospitals. The incidence of hydatidiform mole and GTN at health facilities in the public sector in 2014–2017 was 0.95 per 1000 deliveries and 6.58 per 100 000 deliveries, respectively.

Conclusions: The results suggest that provincial hospitals are important to detect suspected invasive mole and refer to national hospitals for diagnosis and treatment. Further studies on the management of GTD and development of the guidelines of GTD are needed.

Key words: Cambodia, gestational trophoblastic disease, gestational trophoblastic neoplasia, hydatidiform mole, incidence.

Introduction

Gestational trophoblastic disease (GTD) is a group of diseases that originate from trophoblastic cells and consist of hydatidiform mole and gestational trophoblastic neoplasia (GTN). GTN includes invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelial trophoblastic tumor.[1] Hydatidiform mole is an abnormal pregnancy and treatment is conducted by removing molar tissues from the uterus by an evacuation, which is the same as the treatment for miscarriages. The difference between hydatidiform

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moles and miscarriages is the potential of developing invasive mole, which occurs mostly within 6 months after an evacuation for hydatidiform mole.[2–5] When GTN occurs after invasive mole is cured, it is not invasive mole any more but choriocarcinoma.[6] This suggests that invasive mole develops to choriocarcinoma when invasive mole is left without treatment. Choriocarcinoma can metastasize to all organs including the brain, liver, kidney, and intestine, and multi-agent chemotherapy is needed. Therefore, patients with hydatidiform mole need not only treatment but also follow-up after an evacuation to detect invasive mole and prevent developing choriocarcinoma.

It has been reported that the incidence of invasive mole and choriocarcinoma after hydatidiform mole is approximately 15% and 1%, respectively.[2,3,7] Invasive mole can be cured completely by chemotherapy but the mortality of choriocarcinoma is reported to be 15%–20% by multimodal therapy.[7] Ultrasonography, human chorionic gonadotropin (hCG) measurement, and pathological examination, are needed for the management of hydatidiform mole and early detection of invasive mole. The incidence and the mortality of choriocarcinoma may be higher when the management of diseases is not performed appropriately. In developing countries, especially rural and remote areas, health facilities do not have enough resources, such as medical equipment and skilled healthcare workers.[8,9] There are also barriers for patients who want to use health service at health facilities, including financial barriers, distance to health facilities, and low knowledge of health or diseases.[10–12]

Cambodia is a lower-middle income country in South East Asia. The total population has been increasing rapidly since 1980 and reached approximately 16 500 000 in 2019.[13] Total birth in 2019 is estimated to be approximately 365 000.[14] The incidence of hydatidiform mole in Asian countries has been reported to be higher (0.81–4.4 per 1000 live births or pregnancies) compared to Western countries (0.66–1.21 per 1000 pregnancies).[15] To our knowledge, there has been no study on GTDs in Cambodia, including the incidence and the management of GTDs. There is no standard protocol for the management of GTDs in Cambodia. The aim of this paper is to understand the current situation of management of GTD, especially hydatidiform mole, in Cambodia by conducting a questionnaire survey and analyzing Health Information System (HIS) data.

Methods

Questionnaire and participants

A questionnaire was developed to understand the healthcare services for pregnant women and patients with hydatidiform mole in Cambodia. The questionnaire consisted of four parts, including (1) information about the work place of participants (province and name of work place); (2) health services for pregnant patients at their work place (annual numbers of deliveries, operations for spontaneous and induced abortions, and operations for hydatidiform moles); (3) available examinations at their work place (ultrasonography, hCG measurement by machines, and pathological examination); and (4) the experience of treatment for hydatidiform mole. The questionnaire sheet in Khmer language was provided to all 265 attendants at the 16th Annual Conference of the Cambodian Society of Gynecology and Obstetrics (SCGO) on November 17th and 18th in 2017. SCGO is the only one professional society of gynecologists and obstetricians in Cambodia, with 454 members countrywide in 2017.[16] A total of 143 attendants agreed and answered the questionnaire and written informed consent was obtained from each attendant. Seventeen attendants were excluded because 7 attendants worked for administrative offices (operational district, municipal health department, provincial health department) and the category of the working place was not identified in 10 attendants. Finally, 126 attendants were included in the study, which accounted for 27.8% of all SCGO members.

HIS data

Existing health information system in Cambodia covers only the public sector, with three levels of health facilities: health centers, referral hospitals at districts and provinces, and national hospitals. The number of deliveries, spontaneous abortions, induced abortions, hydatidiform moles, and GTNs are reported from all health facilities in the public sector to the Ministry of Health every month using the HIS website.[17] There were 9 national hospitals, 24 provincial hospitals, 68 district hospitals, 1141 health centers in December 2015.[18] Each year, the Department of Planning and Health Information of the Ministry of Health compiled the data according to provinces and the level of health facilities (national hospitals, referral hospitals at operational districts and provinces, and health centers). The annual number of deliveries, spontaneous abortions, induced abortions,

hydatidiform moles, and GTNs from 2014 to 2017 were collected from the HIS database.

Data analysis

The data provided by 126 attendants were analyzed. The work places of the participants were categorized into national hospitals, provincial hospitals, district hospitals, health centers, and the private sector (private clinics and hospitals), and nongovernmental organizations (NGO). There were attendants who worked for the same facilities but answered differently, but all of their answers were included in the analysis. The incidence of hydatidiform mole was calculated per 1000 pregnancies and per 1000 deliveries, and the incidence of GTN was calculated per 100 000 pregnancies and per 100 000 deliveries using the HIS data. Pregnancies included deliveries, spontaneous abortions, and induced abortions. Since all the data did not include any personal information, no ethical approval process was conducted.

Results

Of the 126 participants, most participants were from Phnom Penh ($n = 48$, 38.1%) followed by Kampong Cham Province ($n = 9$, 6.3%), Banteay Meanchey Province ($n = 8$, 5.6%), and Siem Reap Province ($n = 6$, 4.2%) (Table 1, Figure 1). Banteay Meanchey Province is located on the border with Thailand, but it adjoins Siem Reap Province, where the airport is. Participants were from all provinces except Kep Province, Ratana Kiri Province, and Stung Treng Province. Most of the 48 participants from Phnom Penh worked for national hospitals, such as the National Center for Maternal and Child Health ($n = 10$), Khmer Soviet Friendship Hospital ($n = 8$),

Table 1 Province and level of working place of 126 participants

		Public sector					
		National hospital	Provincial hospital	District hospital	Health center	Private/ NGO	Total
Phnom Penh		29	0	1	1	17	48
Provinces		0	42	19	5	12	78
1	Banteay Meanchey	0	3	3	0	2	8
2	Battambang	0	1	0	0	2	3
3	Kampong Cham	0	4	4	0	1	9
4	Kampong Chhnang	0	2	0	0	0	2
5	Kampong Speu	0	3	1	0	1	5
6	Kampong Thom	0	0	2	0	0	2
7	Kampot	0	0	2	0	2	4
8	Kandal	0	5	0	0	0	5
9	Kep	0	0	0	0	0	0
10	Koh Kong	0	1	1	0	0	2
11	Kratie	0	3	1	0	0	4
12	Mondol Kiri	0	1	0	0	0	1
13	Otdar Meanchey	0	3	0	0	0	3
14	Preah Vihear	0	1	0	3	0	4
15	Prey Veng	0	1	0	0	0	1
16	Pursat	0	2	1	0	0	3
17	Ratana Kiri	0	0	0	0	0	0
18	Siem Reap	0	3	0	0	3	6
19	Stung Treng	0	0	0	0	0	0
20	Svay Rieng	0	2	1	0	0	3
21	Takeo	0	2	0	0	1	3
22	Paillin	0	3	0	0	0	3
23	Tbong Kmon	0	0	3	1	0	4
24	Preah Sihaknouk	0	2	0	1	0	3
Total		29	42	20	6	29	126

Abbreviation: NGO, nongovernmental organization.

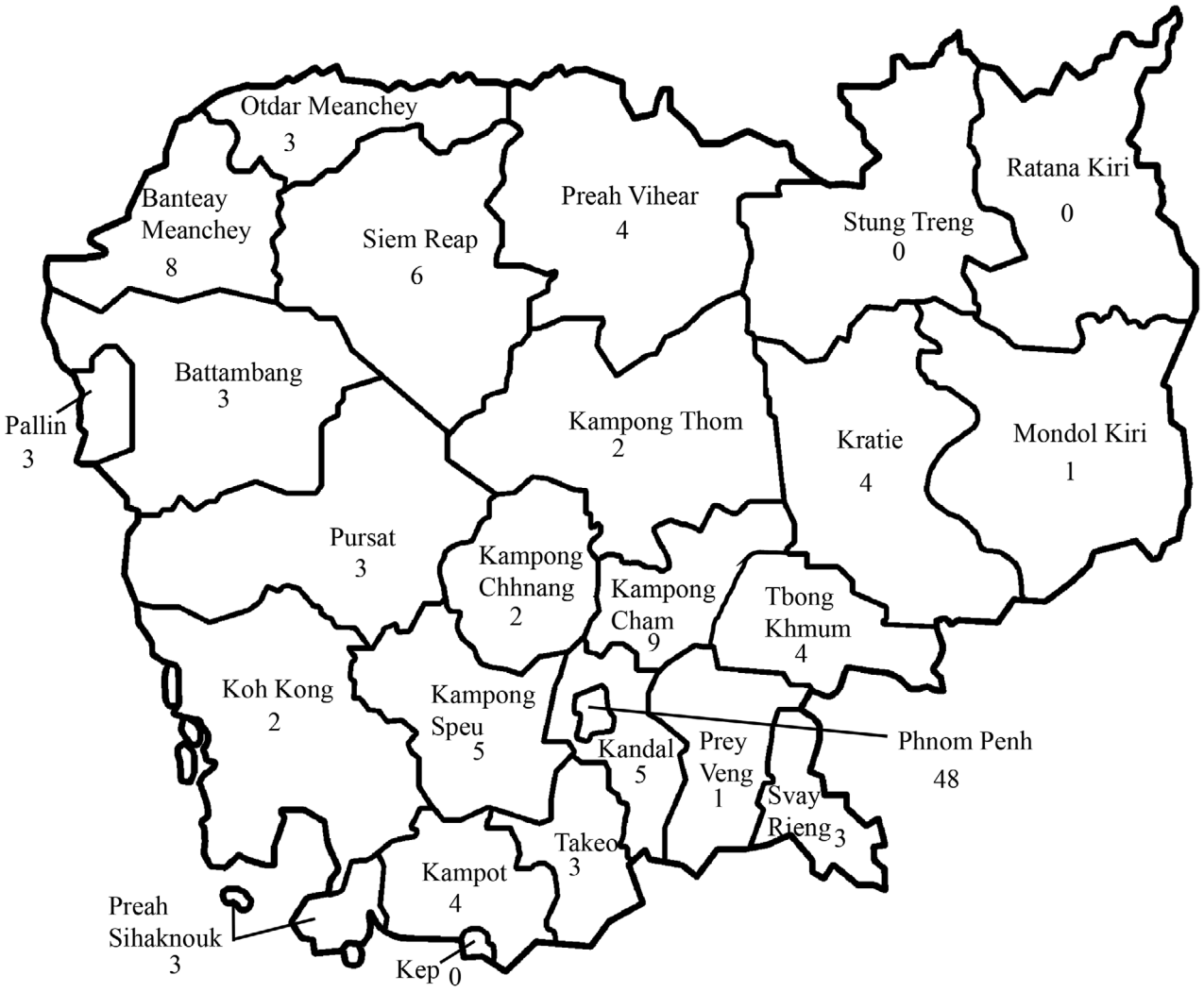

Figure 1 The number of participants who attended the SCGO conference from Phnom Penh and provinces. One hundred twenty-six participants were from all provinces except Kep Province, Ratana Kiri Province, and Stung Treng Province. Most participants were from Phnom Penh followed by Kampong Cham Province, Banteay Meanchey Province, and Siem Reap Province

Preah Kossamak Hospital ($n = 4$), and Calmette Hospital ($n = 3$). There were 78 participants (61.9%) who worked in the provinces and most of the participants worked for provincial hospitals ($n = 42$) followed by district hospitals ($n = 19$). Of the 126 participants, 6 participants were from health centers. There were 29 participants who worked for private clinics and hospitals ($n = 7$), and NGOs that provide health service at their clinics ($n = 22$).

Based on the responses from the participants, healthcare services for pregnant women at each level of health facility in the public sector were compared. Almost all participants answered that their facility provided childbirth service and operations for abortions (Table 2). The annual number of deliveries and abortions varied in each level of facility, but it seemed that higher levels of health facilities had more cases (Table 3). The percentage of participants who answered that they provided treatment for hydatidiform mole was 100% in national hospitals, 90.5% in provincial hospitals, 40.0% in district hospitals but 0% in health centers (Table 2).

An ultrasonography is needed to diagnose pregnancies as well as hydatidiform moles clinically. All

Table 2 Health service for pregnancy and hydatidiform mole according to the level of health facilities in Cambodia

	Public sector				
	National hospital ($N = 29$)	Provincial hospital ($N = 42$)	District hospital ($N = 20$)	Health center ($N = 6$)	Private/ NGO ($N = 29$)
Service related to pregnancy					
Delivery	28 (96.6%)	42 (100%)	19 (95.0%)	6 (100%)	5 (17.2%)
Abortion[a]	27 (93.1%)	42 (100%)	19 (95.0%)	6 (100%)	25 (86.2%)
Hydatidiform mole	29 (100%)	38 (90.5%)	8 (40.0%)	0 (0%)	6 (20.7%)
Examination					
Ultrasonography	26 (90.0%)	41 (97.6%)	19 (95.0%)	0 (0%)	28 (96.6%)
Pathological exam	21 (72.4%)	25 (59.5%)	15 (75.0%)	2 (33.3%)	20 (69.0%)
hCG measurement	15 (51.7%)	0 (0%)	0 (0%)	0 (0%)	8 (27.6%)
Experience of hydatidiform mole	24 (82.8%)	21 (50.0%)	3 (15.0%)	0 (0%)	6 (20.7%)

Abbreviations: hCG, human chorionic gonadotropin; NGO, nongovernmental organization. and [a]Abortion includes spontaneous abortion and induced abortion.

Table 3 The range of annual number of deliveries, abortions, and hydatidiform moles according to the level of health facilities in Cambodia

	Public sector				
	National hospital ($N = 29$)	Provincial hospital ($N = 42$)	District hospital ($N = 20$)	Health center ($N = 6$)	Private/ NGO ($N = 29$)
Delivery	250–12 000	960–5000	350–1440	30–360	20–450
Abortion[a]	36–4000	24–1000	25–1200	5–80	10–2000
Hydatidiform mole	10–300	1–200	1–30	0	1–20

Note: Number in the parenthesis represents the range of annual number in the respondents' answers.; Abbreviation: NGO, non-governmental organization. and [a]Abortion includes spontaneous abortion and induced abortion.

Table 4 The estimated incidence of gestational trophoblastic disease at public health facilities in Cambodia from 2014 to 2017 according to the HIS data

	2014	2015	2016	2017	Total
N of deliveries	303 741	320 127	316 117	321 506	1 261 491
N of pregnancies	320 612	341 672	337 972	342 811	1 343 067
N of HM	298	258	321	316	1193
N of GTN	37	17	8	21	83
Incidence of HM (per 1000 pregnancies)	0.93	0.76	0.95	0.92	0.89
Incidence of HM (per 1000 deliveries)	0.98	0.81	1.02	0.98	0.95
Incidence of GTN (per 100 000 pregnancies)	11.54	4.98	2.37	6.13	6.18
Incidence of GTN (per 100 000 deliveries)	12.18	5.31	2.53	6.53	6.58

Note: Pregnancies included spontaneous abortions, induced abortions, and deliveries. and Abbreviations: GTN, gestational trophoblastic neoplasia; HIS, Health Information System; HM, hydatidiform mole; *N*, number.

of the six participants from health centers answered that their facilities did not have an ultrasonography, but 90.0%–97.6% of participants from national, provincial, and district hospitals answered that their facilities had it (Table 2). Pathological examination is needed for pathological diagnosis of hydatidiform mole and hCG measurement is required to detect the development of invasive mole. Most participants from national hospitals (72.4%), provincial hospitals (59.5%), and district hospitals (75.0%) answered that they can order pathological examinations at their facilities. However, only participants from national hospitals answered that hCG measurement was available at their facilities. The percentage of having an experience of treatment for hydatidiform mole was highest in participants from national hospitals

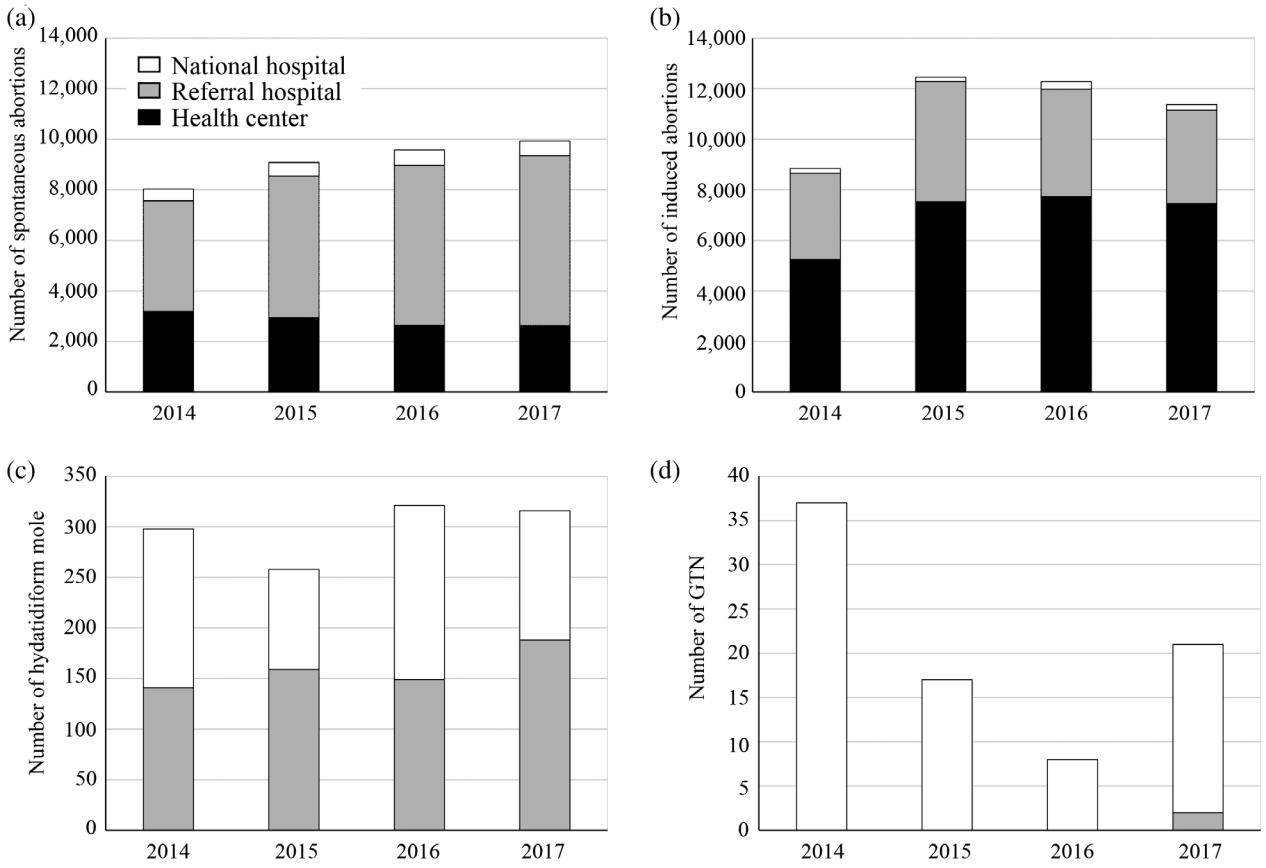

Figure 2 The number of abortions and gestational trophoblastic diseases in the HIS data from 2014 to 2017. Number of spontaneous abortions (a), induced abortions (b), hydatidiform moles (c), and gestational trophoblastic neoplasias (d) are shown according to the level of public health facilities. Referral hospitals include provincial hospitals and district hospitals. The Health Information System (HIS) data included cases reported from all public health facilities in Cambodia. GTN, gestational trophoblastic neoplasia

(82.8%), followed by provincial hospitals (50.0%) and district hospitals (15.0%). There were no participants from health centers who had an experience of treating a hydatidiform mole patient.

Of the 29 participants who worked for the private sector and NGOs, 6 participants (20.7%) answered that their facilities provided treatment for hydatidiform mole; 25 participants (86.2%) answered that their facilities provided abortion operations (Table 2). The percentage of participants who answered that the service was available was 96.6% for ultrasonography, 69.0% for pathological examination, and 27.6% for hCG measurement. Six participants (20.7%) had an experience of conducting hydatidiform mole treatment.

According to the HIS data, the number of deliveries increased from 303 741 in 2014 to 321 506 in 2017 (Table 4). When pregnancies included deliveries, spontaneous abortions, and induced abortions, the number of pregnancies also increased from 320 612 in 2014 to 342 811 in 2017. Between 2014 and 2017, the reported number of hydatidiform mole and GTN ranged from 258 to 321 and from 8 to 37, respectively. The incidence of hydatidiform mole in 2014–2017 was 0.89 per 1000 pregnancies (range, 0.76–0.95) and 0.95 per 1000 deliveries (range, 0.81–1.02). The incidence of GTN varied from 2.37 to 11.54 per 100 000 pregnancies and from 2.53 to 12.18 per 100 000 deliveries, and the average in 2014–2017 was 6.18 per 100 000 pregnancies and 6.58 per 100 000 deliveries.

When the number of reported cases to the HIS data base was compared among three levels of health facilities (national hospital, referral hospital, and health center), most abortions were treated at referral

hospitals followed by health centers (Figure 2). The major facilities for treatment were referral hospitals for spontaneous abortions and health centers for induced abortions. Hydatidiform mole cases were reported from national hospitals and referral hospitals but not from health centers. All GTN cases from 2014 to 2017 were reported from national hospitals except two cases from referral hospitals in 2017.

Discussion

To the best of our knowledge, this is the first report about GTD in Cambodia. The results of this study suggested that the treatment of hydatidiform mole is mainly performed at national hospitals and provincial hospitals. District hospitals and health centers provide operations for spontaneous and induced abortions but not operations for hydatidiform mole. These results suggest that patients are referred from district hospitals and health centers to provincial hospitals when hydatidiform mole is clinically diagnosed. However, all participants from health centers answered that the health centers had no ultrasonography. Recently, it is common in Cambodia for pregnant women to visit different health facilities including private clinics to have an ultrasound examination because they want to be assured about their pregnancy and fetus.[19]

Treatment of GTN and hCG measurement were provided only at national hospitals in Phnom Penh among all public health facilities. Some participants from provincial hospitals (59.5%), district hospitals (75.0%), and health centers (33.3%) answered that pathological examinations were available at their health facilities. Akaba et al. reported that only three national hospitals provided pathological service and there were only 9 pathologists and 16 pathological technicians in 2018.[20] All pathologists worked for national hospitals and the national university in Phnom Penh, but they had dual work at private laboratories which provided pathological service. Doctors in provinces may order pathological examination at private laboratories when patients agree to pay the examination fee. These results suggest that most hydatidiform moles are diagnosed clinically and are not followed up by checking the hCG levels in provinces.

The estimated incidence of hydatidiform mole and GTN in Cambodia was lower than that in neighboring countries. The incidence of hydatidiform mole (per 1000 pregnancies or 1000 deliveries) was reported as 1.9 in Vietnam,[15] 1.70 in Thailand,[21] 1.8 in Thai-Myanmar border,[22] 2.8 in Malaysia,[23] 2.3 in Indonesia,[24] and 2.4 in the Philippines.[25] The incidence of GTN (per 100 000 pregnancies or 100 000 deliveries) was 100 in Thailand[26] and 121 in Indonesia,[24] although fewer studies on GTN were reported compared to studies on hydatidiform mole. The incidence of hydatidiform mole and GTN might be lower than estimated according to the following reasons. First, all GTD cases might not be reported to the HIS database. Inconsistency of reporting was sometimes observed.[27] Second, some hydatidiform moles might be diagnosed as spontaneous abortions without pathological examinations because of the very limited availability of pathological services in the provinces. The low incidence of GTN in this study does not imply good management of hydatidiform mole in Cambodia. Further study is needed to understand the incidence of GTDs in Cambodia by including national hospitals and provincial hospitals.

To prevent the development of choriocarcinoma from hydatidiform mole, suspected cases with invasive mole should be found and referred to national hospitals for diagnosis and treatment of GTN. Private and NGO clinics seem to take part in treatment of hydatidiform mole. Therefore, guidelines of the management (diagnosis, treatment, and follow-up) of hydatidiform mole should be developed for doctors of provincial hospitals and the private clinics. The professional society, SCGO, covers both the public sector and the private sector, therefor; SCGO can play an important role in developing the standard protocol for management of GTD.

Macroscopic diagnosis (hydropic villi <2 mm in a short diameter),[5] routine second curettage,[3,15] hysterectomy for patients who do not hope to have any more pregnancy,[15,28] prophylactic chemotherapy for patients who have risk factors of invasive mole,[15,29] and a pregnancy test are considered to be useful in the hydatidiform mole management in resource-limited settings. Goldstein proposed a positive pregnancy test 8 weeks after evacuations.[30] To develop the guidelines, it is also necessary to understand the management and outcome of invasive mole and choriocarcinoma in Cambodia.

Another problem in the management of hydatidiform mole is that most patients do not visit for follow-up after an evacuation. A registry and follow-up system of post-molar patients can be one of the solutions to this problem. When such a system

was established in Japan in 1962, the registration center called registered patients and their doctors to remind the time of the follow-up. This system was one of reasons which led to a decrease in the incidence of choriocarcinoma after hydatidiform mole and the mortality of choriocarcinoma was successfully reduced in Japan.[31–34] Through this system, both doctors and patients understand the importance of following up after hydatidiform mole, and the incidence of GTD is also understood.

There are some limitations to this study. First, the results of the existing health service in this report may not be completely correct because the results were obtained from only 126 participants using the self-reported questionnaire. Especially, the availability and usage of pathological exam in provinces is questionable. Second, Health services for GTD patients at private and NGO clinics were not clearly identified because only 29 participants from the private sector and NGOs were included in the study. HIS data did not include the data of the private sector. There are many private or NGO clinics and hospitals all over the country. The number of registered private health facilities (in all clinical specialties) is increasing and it was 1258 in 2017, although the estimated number was 4000.[18] According to the Cambodia Demographic Health Survey in 2014, 31.1% of women had childbirths other than public health facilities.[35] Further study including all health facilities in the public sector and private clinics should be conducted to confirm the results in this study.

In Cambodia, treatment of hydatidiform mole is performed at provincial hospitals and national hospitals, while treatment of GTN is provided at only national hospitals in Phnom Penh. The estimated incidence of hydatidiform mole and GTN at all health facilities in the public sector was lower than that in the neighboring countries. The results of this study suggest that it is important for provincial hospitals to find and refer suspected invasive mole to national hospitals. Guidelines on the management of hydatidiform mole are needed for doctors in both the public sector and the private sector, because available health services are limited. Further study on the management and the outcome of GTN is also needed to develop management guidelines.

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Conflict of interest

The authors have nothing to declare.

Data Availability Statement

Data available on request from the authors.

References

1. Albrecht C, Chamley L, Charnock-Jones DS, et al. IFPA meeting 2018 workshop report II: abnormally invasive placenta; inflammation and infection; preeclampsia; gestational trophoblastic disease and drug delivery. *Placenta*. 2019;**84**: 9–13.
2. Yamamoto E, Nishino K, Niimi K, et al. Evaluation of a routine second curettage for hydatidiform mole: a cohort study. *Int J Clin Oncol*. 2020;**25**:1178–86.
3. Kan M, Yamamoto E, Niimi K, et al. Gestational trophoblastic neoplasia and pregnancy outcome after routine second curettage for Hydatidiform mole a retrospective observational study. *J Reprod Med*. 2016;**61**:373–9.
4. Usui H, Qu J, Sato A, et al. Gestational trophoblastic neoplasia from genetically confirmed hydatidiform moles: prospective observational cohort study. *Int J Gynecol Cancer*. 2018;**28**: 1772–80.
5. Kaneki E, Kobayashi H, Hirakawa T, Matsuda T, Kato H, Wake N. Incidence of postmolar gestational trophoblastic disease in androgenetic moles and the morphological features associated with low risk postmolar gestational trophoblastic disease. *Cancer Sci*. 2010;**101**:1717–21.
6. Hirokawa K, Tomoda Y, Kaseki S, Ishizuka T, Nishikawa Y, Goto S. Recurrence of invasive moles and choriocarcinomas. *Asia Oceania J Obstet Gynaecol*. 1986;**12**:11–20.
7. Sato S, Yamamoto E, Niimi K, et al. The efficacy and toxicity of 4-day chemotherapy with methotrexate, etoposide and actinomycin D in patients with choriocarcinoma and high-risk gestational trophoblastic neoplasia. *Int J Clin Oncol*. 2020;**25**:203–9.
8. Fujita N, Abe K, Rotem A, et al. Addressing the human resources crisis: a case study of Cambodia's efforts to reduce maternal mortality (1980–2012). *BMJ Open*. 2013;**3**:e002685.
9. Fujita N, Matsuoka S, Koto-Shimada K, Ikarashi M, Hazarika I, Zwi AB. Regulation of nursing professionals in Cambodia and Vietnam: a review of the evolution and key influences. *Hum Resour Health*. 2019;**17**:48.
10. Chankham T, Yamamoto E, Reyer JA, et al. Knowledge of free delivery policy among women who delivered at health facilities in Oudomxay Province, Lao PDR. *Nagoya J Med Sci*. 2017;**79**:135–45.
11. Koum K, Hy S, Tiv S, et al. Characteristics of antepartum and intrapartum eclampsia in the National Maternal and Child Health Center in Cambodia. *J Obstet Gynaecol Res*. 2004;**30**:74–9.
12. Leak P, Yamamoto E, Noy P, et al. Factors associated with neonatal mortality in a tertiary hospital in Phnom Penh, Cambodia. *Nagoya J Med Sci*. 2021;**83**:113–24.
13. World Bank. Population, total - Cambodia. https://data.worldbank.org/indicator/SP.POP.TOTL?locations=KH

14. *Ministry of Plannning, National Institution of statistics. Population project of Cambodia 2013-2023*. Phnom Penh: National Institute of Statistics; 2017. http://hismohcambodia.org/public/fileupload/PopulationProjection_2023.pdf
15. Yamamoto E, Trinh TD, Sekiya Y, et al. The management of hydatidiform mole using prophylactic chemotherapy and hysterectomy for high-risk patients decreased the incidence of gestational trophoblastic neoplasia in Vietnam: a retrospective observational study. *Nagoya J Med Sci*. 2020;**82**:183–91.
16. Kanal K, Fujita N, Soeung SC, et al. The cooperation between professional societies contributes to the capacity building and system development for prevention and control of cancer in low- and middle-income countries: the practice of cervical cancer prevention and control project in Cambodia. *Glob Health Med*. 2020;**2**:48–52.
17. Department of Planning and Health Information, Ministry of Health. Health Information System Master Plan 2016-2020. 2017. http://hismohcambodia.org/public/fileupload/carousel/HIS-MasterPlan-Nov2017.pdf#search='HIS+Cambodia+Health'.
18. Ministry of Health. *Health information system 2016-2020*. Phnom Penh: MoH; 2017. http://hismohcambodia.org/public/fileupload/carousel/HSP3-(2016-2020).pdf
19. Schantz C, Sim KL, Petit V, Rany H, Goyet S. Factors associated with caesarean sections in Phnom Penh, Cambodia. *Reprod Health Matters*. 2016;**24**:111–21.
20. Akaba H, Fujita N, Stauch G, et al. How can we strengthen pathology services in Cambodia? *Glob Health Med*. 2019;**1**:110–3.
21. Wairachpanich V, Limpongsanurak S, Lertkhachonsuk R. Epidemiology of hydatidiform moles in a tertiary Hospital in Thailand over two decades: impact of the National Health Policy. *Asian Pac J Cancer Prev*. 2015;**16**:8321–5.
22. McGregor K, Myat Min A, Karunkonkowit N, et al. Obstetric ultrasound aids prompt referral of gestational trophoblastic disease in marginalized populations on the Thailand-Myanmar border. *Glob Health Action*. 2017;**10**:1296727.
23. Sivanesaratnam V. The management of gestational trophoblastic disease in developing countries such as Malaysia. *Int J Gynaecol Obstet*. 1998;**60**(Suppl 1):S105–9.
24. Hidayat YM, Darmadi AE, Rachmayati S, et al. Efficacy of oral vitamin a in reducing beta-hCG levels in low-risk gestational trophoblastic neoplasia patients. *Asian Pac J Cancer Prev*. 2020;**21**:3325–9.
25. Cagayan MS. Changing trends in the management of gestational trophoblastic diseases in The Philippines. *J Reprod Med*. 2010;**55**:267–72.
26. Lertkhachonsuk R, Wairachpanich V. Treatment outcomes of gestational trophoblastic neoplasia in King Chulalongkorn Memorial Hospital over two decades. *J Reprod Med*. 2016;**61**:238–42.
27. Long-Hay P, Yamamoto E, Bun S, et al. Outbreak detection of influenza-like illness in Prey Veng Province, Cambodia: a community-based surveillance. *Nagoya J Med Sci*. 2019;**81**:269–80.
28. Zhao P, Lu Y, Huang W, Tong B, Lu W. Total hysterectomy versus uterine evacuation for preventing post-molar gestational trophoblastic neoplasia in patients who are at least 40 years old: a systematic review and meta-analysis. *BMC Cancer*. 2019;**19**:13.
29. Wang Q, Fu J, Hu L, et al. Prophylactic chemotherapy for hydatidiform mole to prevent gestational trophoblastic neoplasia. *Cochrane Database Syst Rev*. 2017;**9**:CD007289.
30. Goldstein DP. Prophylactic chemotherapy of patients with molar pregnancy. *Obstet Gynecol*. 1971;**38**:817–22.
31. Goto S, Ino K, Mitsui T, et al. Survival rates of patients with choriocarcinoma treated with chemotherapy without hysterectomy: effects of anticancer agents on subsequent births. *Gynecol Oncol*. 2004;**93**:529–35.
32. Takeuchi S. Incidence of gestational trophoblastic disease by regional registration in Japan. *Hum Reprod*. 1987;**2**:729–34.
33. Hando T, Ohno M, Kurose T. Recent aspects of gestational trophoblastic disease in Japan. *Int J Gynaecol Obstet*. 1998;**60** (Suppl 1):S71–S6.
34. Kawashima Y, Maeda M, Fujii T. Registry and follow-up systems of trophoblastic disease in Japan. *Semin Surg Oncol*. 1985;**1**:84–94.
35. National Institute of Statistics, Directorate General for Health, ICF International. *Cambodia demographic and health survey 2014*. Phnom Penh, Cambodia, and Rockville, Maryland, USA: National Institute of Statistics, Directorate General for Health, and ICF International; 2015.