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EPIDEMIOLOGY

Type 1 diabetes in Laos, 2016–2021

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Abstract

Objective: Before 2016, no child was known to survive type 1 diabetes (T1D) in Laos, a lower-middle income country (LMIC) in South-east Asia. In partnership with the Laos government, a non-government organization (NGO) called Action4Diabetes (A4D) has since been providing insulin, blood glucose monitoring kits, HbA1c testing, and emergency hospital expenses for Laotian children and young people (CYP) with T1D, and education for healthcare professionals. Here, we report the demographics and clinical outcomes of the CYP with T1D enrolled in A4D's Clinic Support Programme.

Research Design and Methods: We collated and analyzed data on all known CYP with T1D in Laos, including gender, age and presentation at diagnosis, duration of diabetes, hospital admissions, and glycemic control during follow-up.

Results: Fifty-three CYP (30 male; 57%) were diagnosed with T1D at a mean age of 11.3 years. Thirty CYP (57%) presented in diabetic ketoacidosis (DKA) at diagnosis. As at 16 August 2021, mean duration of T1D was 2.3 years. Forty-five CYP (85%) remained on active follow-up. Mean HbA1c for all 53 CYP was 8.7% (72 mmol/mol). Average HbA1c for the CYP in the age ranges of 1–5 years, 6–10 years, 11–15 years, 16–20 years, and 21–25 years, was 7.9% (63 mmol/mol), 8.2% (66), 8.4% (68), 9.4% (79), and 8.4% (68), respectively.

Conclusions: This is the first report on the status of T1D care in Laos, achieved through close partnership between the government and an NGO from 2016 to 2021. More global efforts to improve T1D care outcomes in Laos and other LMICs are urgently needed.

KEYWORDS

Laos, lower-middle income country, non-government organization, type 1 diabetes

1 | INTRODUCTION

It has been more than 100 years since the hormone insulin was first isolated and used as a life-saving treatment for patients with type 1 diabetes (T1D).[1] Yet, access to insulin is still limited for many patients around the world.[2] A recent editorial in *The Lancet Diabetes & Endocrinology* brought home this issue, that even in the year 2021, it remains an unfulfilled hope to make insulin available for all who need the treatment.[3] Sadly, lack of access to insulin is the main cause of mortality for a child with T1D globally.[4,5] The *Lancet* Commission on

diabetes 2020[6] estimated that more than 14,000 children and young people (CYP) with T1D worldwide died in 2017. Many more CYP have probably perished because this grave statistic was derived from very sparse data on diabetes outcomes for the countries within South-east Asia (SEA) and absolutely no data at all for the Lao People's Democratic Republic (Laos).

Laos is a lower-middle income country (LMIC) in SEA with a population of 7,276,000.[7] In 2020, its gross domestic product (GDP) per capita was USD2,542,[7] of which only 2.5% or the equivalent of USD63.55, was spent by the government on healthcare.[7] Laos has 0.4 doctors per 1000 of its population,[7] compared to 2.8 per 1000 in the United Kingdom.[8] In Laos, universal health coverage for diabetes does not include insulin treatment and self-monitoring of blood glucose (SMBG). Before 2016, no Laotian child was known to have survived T1D into adulthood. Since 2016, in partnership with the Laos government, a non-government organization (NGO) called Action4Diabetes (A4D)[9,10] has been providing diabetes treatment for Laotian CYP with T1D, including insulin, SMBG kits, HbA1c testing and emergency hospital expenses, as well as education on the management of T1D for Laotian healthcare professionals.

In this paper, we report for the first time the demographics of all Laotian CYP with T1D who were enrolled in the A4D programme between February 2016 and March 2021, and their clinical outcomes from the time of enrolment until 16 August 2021.

2 | METHODS

2.1 | Study design, population, and setting

Since its inception in 2015, A4D's Clinic Support Programme has been assisting CYP with diabetes across six countries in SEA, namely Cambodia, Laos, Malaysia, Myanmar, Thailand, and Vietnam.[9] To systematically track the outcomes and monitor the progress of these CYP, A4D maintains a database detailing relevant information pertaining to the diabetes care of each individual who is enrolled into the A4D programme. Data are collected at each site by the local named healthcare professionals. Data entry activities take place continually and are closely monitored and reviewed monthly by the A4D data coordinator and the A4D regional manager.

This study focused on Laotian patients in the A4D programme. Laos has 5 main hospitals and 134 district hospitals across its 17 provinces and Vientiane Capital City prefecture. We included all the Laotian CYP who were enrolled since the first patient in February 2016 until the most recent patient in March 2021. All the patients were enrolled at or within 2 months of being diagnosed with diabetes, and had been treated using twice daily injections of pre-mix insulin. They were also provided with blood glucose testing kits to perform SMBG.

All the data in this study were collated from the A4D database as at 16 August 2021, anonymized and de-identified before analysis was conducted by the study team. The three doctors in Mahosot Hospital in Vientiane, Laos, who co-authored this report, confirm that the Research Ethics Committee at the University of Health Sciences, Laos, reviewed and approved the study. They were directly involved in patient recruitment and consent taking, data collection and extraction as well as de-identification of the patients. Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans.

2.2 | Patient demographics at diagnosis

The province in Laos from which each patient had originated was extracted from the A4D database. Demographic information also included the patient's gender, age at diagnosis, HbA1c at diagnosis, and whether the patient was in diabetic ketoacidosis (DKA) at diagnosis of diabetes. As measurement of T1D-associated autoantibodies was not available in Laos, the CYP were clinically diagnosed with T1D if they first presented acutely at an age older than 6 months and had signs and symptoms that were characteristic of T1D.[11]

2.3 | Diabetes care outcomes during follow-up

The A4D database prospectively records each enrolled patient's diabetes care outcomes. We extracted outcomes including whether patient was still on active follow-up in the A4D programme, and if not, whether patient was lost to follow-up or known to have died; and all hospital admissions and the reasons for admission (DKA, severe hypoglycemia, or other reasons) for the entire period during which each patient was on active follow-up.

Additionally, the patients had HbA1c measured and recorded in the A4D database up until May 2021. HbA1c was measured using CLOVER A1c™ Self Test Analyser (Infopia Co. Ltd., Korea) in Mahosot Hospital's clinical biochemistry laboratory, and reported in both % NGSP (National Glycohemoglobin Standardization Program)[12] and mmol/mol IFCC (International Federation of Clinical Chemistry) standardization.[13]

2.4 | Data analysis and summary statistics

We entered all the anonymized data into a Microsoft Excel spreadsheet, and computed all summary statistics using its built-in formulae and generated all graphs and charts using its chart wizards.[14] The mean and standard deviation (SD) of continuous variables, including age of patient at diagnosis, current age of patient, duration of T1D, and HbA1c, were expressed to one decimal place.

For this report, we derived the following summary statistics on HbA1c:

1. The mean and SD of all the patients' HbA1c at diagnosis of T1D.
2. The mean and SD of all the measured HbA1c in the patients during follow-up, for the entire study period as well as broken down yearly. As there were patients in this study who did not have any HbA1c measured during their follow-up, we separately calculated

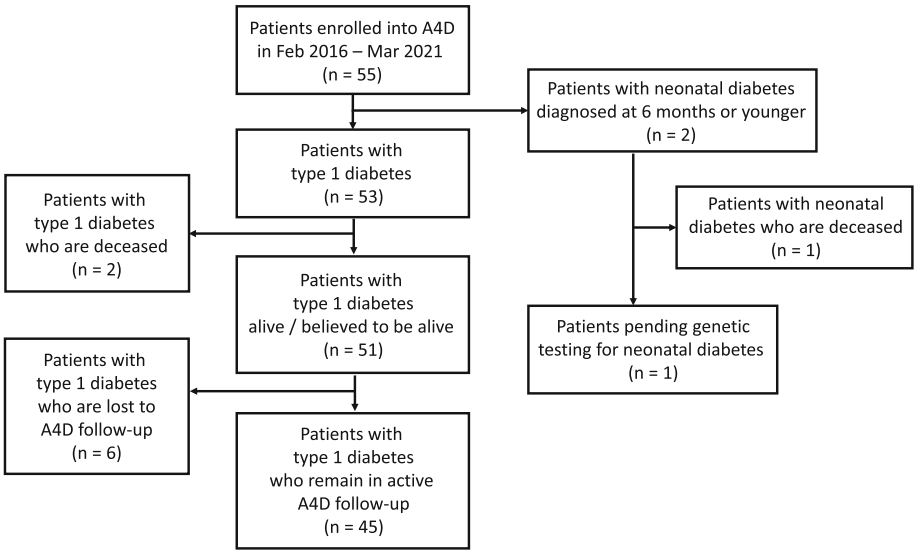

FIGURE 1 Patients with diabetes enrolled in the A4D programme in Laos, 2016–2021. Flow diagram showing all the patients who have been enrolled into the A4D programme between February 2016 and March 2021

the average HbA1c of those patients who had at least one HbA1c measurement.

3. It has been consistently reported that the glycemic control of CYP with T1D can vary quite markedly with age during childhood through adolescence and young adulthood in Western populations.[15–17] The same observation has recently been made in Thailand, a neighboring country to Laos in SEA.[18] To explore whether the same pattern of variation in HbA1c can also be found in our study, we categorized the HbA1c of each of the Laotian patients into five age groups (1–5 years old; 6–10 years old; 11–15 years old; 16–20 years old; and 21–25 years old) based on the age at which each of their HbA1c was done. We then computed the average HbA1c for each patient, and reported the mean and SD of the average HbA1c for all the patients within each of the five age groups.
4. Finally, we calculated the number (*n*) and proportion (%) of Laotian CYP with T1D who had average HbA1c <7.5% (<58 mmol/mol), 7.5%–9.5% (58–80 mmol/mol), and >9.5% (>80 mmol/mol), by each year of the study period 2016–2021 and by the above five age groups.

3 | RESULTS

3.1 | Enrolment and geographical distribution of 55 patients with diabetes

A total of 55 CYP were diagnosed with diabetes in Laos and enrolled into the A4D programme between February 2016 and March 2021 (Figure 1). Two of the patients were diagnosed before 6 months old and were presumed to have neonatal diabetes and not T1D; one of these patients had died and the other patient was pending genetic testing for neonatal diabetes. The remaining 53 CYP were clinically diagnosed with T1D. Table S1 provides a detailed yearly breakdown of the number of patients who were enrolled, in active follow-up, lost to follow-up, and had passed away, in the period 2016–2021.

As shown in Figure 2, the CYP who were enrolled into the A4D programme originated from almost all parts of Laos. Twenty-three of the 55 CYP (42%) were from Vientiane Capital City prefecture, and the other 32 (58%) were from 14 of the 17 Laotian provinces. Fifty-four of the 55 CYP (98%) were receiving follow-up diabetes care at the main Mahosot Hospital in Vientiane, the capital city of Laos. There was 1 CYP with T1D who was receiving follow-up diabetes care at Laos Friends Hospital for Children in Luang Prabang province. The geographical distribution of patients in Figure 2 clearly shows that the patients who had been lost to follow-up or had passed away came from provinces that were located in the northern and southern parts of Laos, and furthest away from Vientiane.

3.2 | Study population of 53 patients diagnosed with T1D

Of the 53 CYP with T1D who were enrolled in the A4D programme during the study period, 30 (57%) were male and 23 (43%) were female (Table 1). The CYP were diagnosed between 1.9 years old and 21.8 years old, with a mean (SD) age of 11.3 (4.3) years. At diagnosis of T1D, the boys were about 1.6 years younger than the girls; 30 patients (57%) were in DKA, including 19 of the 30 boys (63%) and 11 of the 23 girls (48%); and mean (SD) HbA1c was 12.7 (2.0) % or 115 (22) mmol/mol.

3.3 | Outcomes of patients with T1D

As at 16 August 2021, overall mean (SD) duration of T1D was 2.3 (1.5) years; 2.0 (1.4) years for the 30 boys and 2.7 (1.7) years for the 23 girls. Forty-five of the 53 CYP with T1D (85%) remained in active follow-up in the A4D programme, comprising 24 of the 30 boys (80%)

FIGURE 2 Geographical distribution of patients with diabetes enrolled in the A4D programme in Laos, 2016–2021. Map showing the number of patients with diabetes enrolled into A4D to-date in each of the 17 provinces of Laos as well as the Vientiene Capital City prefecture which has the largest number of patients enrolled so far. Where applicable, the number of patients who are lost to follow-up is denoted in (*) and those who have deceased are denoted as (**). All the patients were clinically diagnosed to have type 1 diabetes, except for two patients who were diagnosed at 6 months or younger and are presumed to have neonatal diabetes; one of them is denoted as (1^{n}) and the other one has died (1^{n}**)

and 21 of the 23 girls (92%). Mean (SD) current age of these 45 CYP was 13.8 (4.9) years; the boys were 12.3 (4.5) years old and the girls were 15.4 (5.0) years old. Another 6 CYP with T1D (5 boys and 1 girl) were lost to follow-up, and 2 CYP with T1D (1 boy and 1 girl) had passed away (Table 1). Since diagnosis of T1D, 32 of the 53 CYPs (60%) had required hospital admissions for DKA, 8 (15%) for severe hypoglycemia, and 7 (13%) for various reasons, including pneumonia, urinary tract infections, eye complications and pancreatic calcifications (Table 1).

3.4 | HbA1c during follow-up

Detailed computations of all HbA1c statistics are provided in Table S2 and plotted in Figure S3. During follow-up in the A4D programme, the CYP with T1D had a total of 262 HbA1c measurements. Overall mean (SD) HbA1c was 8.7 (2.4) % or 72 (26) mmol/mol. Five of the 53 CYP with T1D (9%) did not have any HbA1c done. The other 48 CYP with T1D (91%) had an average of 4.9 HbA1c measurements during their entire follow-up, or an average of 1.9 HbA1c measurements per year

TABLE 1 Patients with type 1 diabetes enrolled in the A4D programme in Laos at diagnosis and their follow-up status as of 16 August 2021

	Male ($n = 30$)	Female ($n = 23$)	All patients ($n = 53$)
At diagnosis			
Age, years (mean ± SD)	10.6 ± 3.6	12.2 ± 4.9	11.3 ± 4.3
DKA at onset, *n* (%)	19 (63%)	11 (48%)	30 (57%)
HbA1c (mean ± SD)			
NGSP (%)	12.7 ± 1.7	12.6 ± 2.4	12.7 ± 2.0
IFCC (mmol/mol)	115 ± 19	114 ± 26	115 ± 22
Current status			
Active follow-up, *n* (%)	24 (80%)	21 (92%)	45 (85%)
Lost to follow-up, *n* (%)	5 (17%)	1 (4%)	6 (11%)
Deceased, *n* (%)	1 (3%)	1 (4%)	2 (4%)
Duration of type 1 diabetes			
For all enrolled patients, years (mean ± SD)[a]	2.0 ± 1.4	2.7 ± 1.7	2.3 ± 1.5
Current age			
For patients on active follow-up, years (mean ± SD)[b]	12.3 ± 4.5	15.4 ± 5.0	13.8 ± 4.9
Reason for hospital admission			
DKA, *n* (%)	20 (67%)	12 (52%)	32 (60%)
Severe hypoglycemia, *n* (%)	4 (13%)	4 (17%)	8 (15%)
Other reasons, *n* (%)	4 (13%)	3 (13%)	7 (13%)

Abbreviations: DKA, diabetic ketoacidosis; IFCC, International Federation of Clinical Chemistry; NGSP, National Glycohemoglobin Standardization Program; SD, standard deviation.

[a]All the patients were enrolled into A4D at or within 2 months of diagnosis of type 1 diabetes.

[b]45 patients with type 1 diabetes (24 boys and 21 girls) remained in active follow-up.

of follow-up (range 0.8–3.8). These CYP's average HbA1c was 8.6% (71 mmol/mol). When the CYP were categorized into age ranges of 1–5 years, 6–10 years, 11–15 years, 16–20 years, and 21–25 years at the time when they had the HbA1c performed, average HbA1c was 7.9% (63 mmol/mol), 8.2% (66 mmol/mol), 8.4% (68 mmol/mol), 9.4% (79 mmol/mol), and 8.4% (68 mmol/mol), respectively. Across all age groups, majority of the CYPs had an average HbA1c greater than 7.5% (58 mmol/mol).

4 | DISCUSSION

This is the first ever report on the status of T1D care in Laos. As at 16 August 2021, 45 of the 53 CYP with T1D who were enrolled in A4D's Clinic Support Programme constituted the first known cohort of Laotians to have survived the diagnosis of T1D. Given that as recently as 2016, no child was known to have lived with T1D into adulthood in Laos, this is indeed a remarkable achievement for the LMIC in SEA.

However, this study clearly highlights that Laos faces the same difficulties as the ones encountered in many LMICs, where the costs of diabetes treatment are often prohibitive,[19] and access to skilled and trained healthcare professionals is limited due to resource constraints. As patients with T1D need insulin for survival, limited access to insulin clearly leads to unnecessary mortality, while survivors have poor glycemic control and potentially suffer from T1D-related complications due to unavailability of blood glucose monitoring kits.[20] Disparate healthcare financing and insurance models, complexities in logistics affecting transport, distribution and supply chains, and lack of transparency in pricing among manufacturers of insulin, all add up to further threaten and compromise T1D care in LMICs.[21] In the case of Laos, the first steps to overcoming the multitudes of barriers to T1D care were taken through partnership between A4D and the Laotian government in 2016. The outcome data suggest that there is still much more that needs to be done.

We found that 57% of the Laotian CYP presented in DKA at the onset of T1D, compared to lower rates ranging from 19.5% to 43.8% among 59,000 children with newly diagnosed T1D in Europe, North America, and Australia in 2006–2016.[22] The exact reasons for the disparity were not the subject of investigation in this study. However, it would be reasonable to attribute the higher DKA rates at diagnosis among the Laotian CYP to factors such as the lack of awareness of T1D in the general Laotian population and the long distances that patients need to travel to reach a hospital for medical attention, thereby leading to late presentation at disease onset. Indeed, we observed that geographical distance from the Laotian capital city was inversely correlated with desirable T1D care outcomes. Many patients had to make overland round trip journeys that exceed 24 hours in order to access appropriate medical care in the capital city, Vientiane. There is a need to enlist more hospitals and healthcare professionals in Laos to participate in the A4D programme so that Laotian CYP can receive T1D care and support nearer to their hometowns.

During 2016–2021, the glycemic control of the Laotian CYP with T1D varied with age during childhood through adolescence and young adulthood in a similar pattern as several other populations of CYP with T1D[15–18] and was particularly suboptimal among those aged 16–20 years old, whose average HbA1c was 9.4% (79 mmol/mol). Collectively, the HbA1c statistics that were derived in this study would place Laos in the "intermediate care" tier of T1D outcomes as proposed by Ogle and colleagues.[23] While it is noteworthy that this level of care was attained within a short span of only 5 years of the A4D programme in the country, majority of the Laotian CYP with T1D did not meet the HbA1c target of <7.5% (58 mmol/mol) as recommended by the International Society for Pediatric and Adolescent Diabetes (ISPAD), or <7% (53 mmol/mol) where access to comprehensive care is available.[24] This is not surprising because all the CYP with T1D in Laos were using twice-daily insulin regimen during the study period. Previously, other authors have observed that patients with T1D in less-resourced Asian countries who were on no more than two insulin injections per day had mean HbA1c values that were even higher than this current Laotian cohort.[25] A4D was able to provide the Laotian CYP with insulin analogs, but conversion to more intensive insulin regimens had been constrained by two inter-related factors: (1) the lack of availability of insulin analogs because insulin manufacturers were reluctant to market the products in Laos due to low demand; and (2) the lack of knowledgeable healthcare professionals in Laos who could conduct T1D self-management education and provide ongoing support for patients in terms of carbohydrate counting and matching bolus insulin doses with meals. In the coming years, education of physicians and family members to empower patients in self-care would be key to improving T1D care outcomes in Laos.

Our study has a few limitations. First, the A4D programme in Laos comprised a relatively small number of patients with short follow-up periods to-date, and given the small sample size, we avoided performing further data analysis that might lead to erroneous conclusions. Second, the diagnosis of T1D in Laos was based solely on clinical features at presentation, including an age of older than 6 months, without checking for autoimmune markers associated with T1D. Third, there was a lack of important data that could inform the reasons for suboptimal glycemic control in the Laotian patients, such as the number of SMBG that the patients had actually been able to perform each day. Fourth, the outcomes of the 6 patients who had been lost to follow-up were unclear, and one could only speculate whether it was a mere coincidence that 5 of the 6 patients were boys, i.e. 17% of the 30 boys with T1D, compared to just one female patient (4% of the 23 girls). Lastly, we were unable to find evidence that there was any surviving Laotian who was living with T1D but not enrolled in the A4D programme during the study period; however, we could not be totally certain because there is no published nor publicly available information.

5 | CONCLUSIONS

What has been achieved in Laos during 2016–2021 demonstrates that close partnership between governments and NGOs has enormous potential in developing sustainable and locally owned solutions for diabetes care in CYP with T1D residing in LMICs. In addition to providing insulin and blood glucose test kits for patients, supporting the education for healthcare professionals is also crucially important. While much progress has been made within a short time in Laos, more global efforts to improve T1D care outcomes in LMICs are urgently needed.

AUTHOR CONTRIBUTIONS

Ngee Lek conceptualized the study, developed the methodology, formulated and performed the data analyses, interpreted the findings, and drafted the manuscript. Amphayvanh Manivong, Khaysy Rassavong and Daoheuang Phommachack contributed to the data collection, extraction and de-identification. Charles Toomey conceptualized the study and provided leadership responsibility for the research. Sze May Ng conceptualized the study, developed the methodology, and interpreted the findings. All authors critically revised the manuscript for important intellectual content, approved the final manuscript as submitted, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST

Charles Toomey is one of the co-founders of Action4Diabetes. Sze May Ng and Ngee Lek serve as voluntary medical advisors of Action4Diabetes. All the authors declare no other conflict of interests.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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