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ORIGINAL ARTICLE

Prevalence of epilepsy in the rural area of the Bolivian Gran Chaco: Usefulness of telemedicine and impact of awareness campaigns

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Abstract

Objective: The objective of this study is to estimate the prevalence of epilepsy with Tonic–Clonic (TC) seizures in rural areas of the Bolivian Gran Chaco and to evaluate the usefulness of telemedicine in this context.

Methods: The study was carried out in the Isozo Area, southern-eastern Bolivia. Twenty-five rural communities with a population of 8258 inhabitants were included in the survey. Trained community-health workers administered a validated single screening question to the householders (stage I). A second face-to-face questionnaire was administered to each positive subject (stage II). At stage II subjects were also screened using the smartphone app "Epilepsy Diagnosis Aid". Subjects screened positive at stage II underwent a complete neurological examination to confirm the diagnosis (stage III). Due to the COVID-19 lockdown, some subjects have been evaluated through a digital platform (Zoom®).

Results: One-thousand two-hundred and thirteen interviews were performed at stage I, corresponding to a total screened population of 6692 inhabitants. Thirty-eight screened positive were identified at stage I and II and of these, 28 people with epilepsy were identified, giving an overall prevalence of 4.2/1000 (95% CI 2.6–5.7). Prevalence rate steeply increased with age reaching a peak of 7.9/1000 in the population aged 20–29 years without significant differences between women and men. For almost 50% of the screened positive subjects, confirmation of epilepsy by a neurologist at stage III was achieved through simple videoconsultation. After a simultaneous awareness campaign, 22 self-reported PWE requested a consultation and, among them, 11 had a diagnosis of epilepsy confirmed.

Valeria Todaro, Loretta Giuliano, contributed equally to the manuscript.

Significance: This study shows a prevalence estimate close to those reported for LMIC. Simple videoconsultation and specific apps may be valuable tools in epidemiological research. Awareness campaigns are important allies for a full case identification, particularly in contexts where higher rates of stigma are recorded.

KEYWORDS
epilepsy, telemedicine, tropical health

1 | INTRODUCTION

Epilepsy is one of the most common neurological diseases, that affects more than 65 million people worldwide[1] accounting for an estimated 0.7% of the global burden of diseases.[2] More than 80% of people with epilepsy (PWE) live in low- and middle-income countries (LMIC), where the disease remains largely untreated.[1] A variable percentage of PWE worldwide do not receive appropriate and comprehensive treatment, a phenomenon known as epilepsy treatment gap (ETG). ETG ranges from 9.8% in high-income countries to 66.3% in upper-middle income countries, 70.3% in LMIC and 86.9% in low-income countries, with great variability within countries.[3] In Latin American countries, a treatment gap (TG) of 60.6% (95% CI 45.3–74.9) was estimated in 2013, with high differences between rural (77.8%; 95% CI 67.4–86.8) and urban (26.2%; 95% CI 10.2–46.4) areas.[4]

Epidemiological studies are the principal instruments to identify health care priorities for planning primary interventions and allocating health resources. In this context, prevalence studies are largely used.[4] To estimate the prevalence of epilepsy in LMIC, particularly in rural areas, the two-stage door-to door design is considered the gold standard,[5] but these studies are costly to implement in large and remote populations. In this design, the first stage consists of a face-to-face interview of the whole target population performed by community health workers (CHWs) and takes considerable time; the second stage requires a diagnostic confirmation by neurologists, rarely available in these areas and that must assess a large number of false-positive subjects. Moreover, the inaccessibility of the territory and cultural barriers make this effort particularly difficult. However, the more the areas are geographically and culturally inaccessible, the more interventions are needed to reduce the treatment gap. As highlighted by the WHO, in this context the detection of epilepsy with tonic–clonic (TC) seizures by the CHWs represents the main priority, since TC seizures are associated with higher comorbidity, injury and mortality than non-convulsive epilepsy.[6] An alternative design to detect TC seizures is represented by the three-stage design.[7–9] In this study design, the screening phase is performed interviewing the householder rather than the entire population, using a single standardized question to detect TC seizures; the second stage consists of a brief standardized interview to the suspected cases who, if positive, will be evaluated by a neurologist for the diagnosis confirmation. Such a design reduces the number of face-to-face interviews leading to a large time and cost reduction. Moreover, TC seizures can be easily identified by CHWs because of their clear clinical manifestations with a consequent reduction of the number of false positives.

Key Point

1. Prevalence of epilepsy in the rural areas of the Gran Chaco region is stable compared with previous surveys in the same area.
2. Simple videoconsultation and smartphone applications may be valuable tools in epidemiological research.
3. Awareness campaigns are important allies for a full case identification, particularly in contexts where higher rates of stigma are recorded.

Recently, the use of technology began to spread in epidemiological contexts. An increasing number of smartphone applications to assist in the process of diagnosis for different diseases have been implemented. Among those, the "Epilepsy diagnosis Aid" app has been developed for trained CHWs, to confirm the diagnosis of PWE in LMIC, showing a good agreement between the probability score of epilepsy obtained and the neurologists' diagnoses.[10] This kind of tool may be useful also in epidemiological surveys to improve the accuracy during the screening phase. On the other side, simple videoconsultation has been proposed as an effective way to assess suspected cases and guide patient's diagnosis and treatment. Its use has seen a dramatic increase during the COVID-19 pandemic, improving digital skills among medical personnel, also in the areas where digital tools are not widely available.[11] In LMIC, particularly in rural areas, the confirmation of suspected epilepsy cases, or of those screened positive in case

of epidemiological surveys, is often difficult due to the lack of neurologists. In this setting, the use of simple videoconsultation may contribute not only to the feasibility of epidemiological surveys, reducing time and costs, but may also improve the access to diagnosis. However, no studies have been conducted to date to establish the usefulness of telemedicine in epidemiological studies on epilepsy in LMIC. The aim of our study was to estimate the prevalence of epilepsy with TC seizures in rural areas of the Bolivian Gran Chaco. We also evaluated the usefulness of telemedicine as a possible aid for epidemiological studies in LMIC.

2 | MATERIALS AND METHODS

2.1 | Study area

The study has been conducted in the Chaco area of the Plurinational State of Bolivia, which is a LMIC where about 4 million people live under the "poverty line"[12] and where the access to the health system is still difficult, particularly in the rural areas.[13]

The southeast region of Bolivia is part of the "Gran Chaco," a subtropical area also including Argentina and Paraguay. The ethnic group living in the study area is mainly represented by native Guaraní people, living in poor dwellings located in rural communities often reachable only by rural roads, without running water or electricity, and with a local economy based on agriculture and animal husbandry. The study was carried out in the Isozo area, a rural area located in the Cordillera Province, Department of Santa Cruz composed by 25 rural communities located far from each other and very distant from the urban context.

2.2 | Study population

The study included all the 25 rural communities located in the Isozo area. According to the 2019 census, the total population living in this area is of 8258 people in 25 communities, 4346 men and 3912 women, most of them represented by indigenous Guaraní. Racially, the population is a mixture of mestizos, descendants of intermarriage between Spanish colonists and the native tribes (the Guaranì-Chiriguanos), and approximately 30% pure Guaraní Indians. The majority of the population speaks both Spanish and Guaraní; a minority speaks only Guaraní.

2.3 | Study design

The study began on September 2019 and was completed on May 2021, during the outbreak of COVID-19 pandemic. A three-stage door-to-door survey was carried out, using a Spanish-language screening tool to detect TC seizures, previously validated in the same area.[7] During the same period, as part of a larger project, to improve knowledge about epilepsy, educational and community awareness campaigns have been carried out in this area. Awareness campaigns were hold in the rural communities by a local anthropologist and a specialized nurse and were directed toward representative members of the local population. Educational and awareness campaigns were performed using the same study designs of those previously carried out by our group in other similar areas of the Bolivian Gran Chaco.[14–16]

2.4 | Stage I

The screening was conducted by previously trained CHWs, living in the communities involved in the study. The first section of the questionnaire consisted in a single screening question administrated to the householders (the head of the family or the most reliable person available) to identify any possible case within the family.

2.5 | Stage II

In the second section, all the people identified at stage I (or someone for them if unable to answer by themself or if under 12 years old) were administered a more specific questionnaire, that included one main question and five adjunctive questions for those who answered yes to the first one (Appendix S1 and S2). A 13-question questionnaire using the app Epilepsy diagnosis Aid (developed by NetProphets Cyberworks Pvt. Ltd.) was also administered by trained CHWs. This app gives the probability that an episode of altered consciousness is due to an epileptic seizure based on the answers to the questions, providing an interpretation of the probability score obtained (Appendix S3). In particular, subjects who obtain scores >80 are considered as "having epilepsy" and those with scores <31 as "not having epilepsy" with the others classified as uncertain.[17] This app has been previously used in the Bolivian Gran Chaco, with a sensitivity of 92.1% (95% CI 78.6–98.3) for the identification of all epilepsy types and 94.3% (95%CI 80.8–99.3) for epilepsy with TC seizures.[18]

2.6 | Stage III

Those screened positive at stage II underwent a neurological evaluation to confirm or exclude the diagnosis. Due to COVID-19 emergency safety measures, on-site

consultations have been forbidden for non-urgent cases. In order to continue the diagnostic workup, when necessary, neurological consultations have been performed through a digital platform (Zoom®). For simple videoconsultation, patients were admitted at the rural health centers, where a CHW was responsible to mediate between the specialist neurologist and the patient, while the neurologist (EC) performed the simple videoconsultation directly from Santa Cruz de la Sierra where she was working. A complete clinical history was taken and a full neurological examination was made during the on-site consultation. During simple videoconsultation, a complete clinical history was collected. Concerning the neurological examination, basic examination was made, with the help of a local CHW, with evaluation of mental status, language, cranial nerves function, and basic evaluation of motor function (strength and coordination). The duration of the consultation was similar in both settings. Rural health centers were provided of computer and stable internet connection. When the computer could not be used, a smartphone was used in its place.

2.7 | Epilepsy definition

According to the ILAE, epilepsy was clinically defined as a "condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause."[5,19] We defined TC seizures as "episodes characterized by loss of consciousness lasting more than 1 minute, presence of tonic movements (such as generalized stiffening) and/or clonic movements (such as thrashing about) and at least one of the followings: (1) sphincter disturbance (i.e. loss of urine or stool during the fit); (2) muscle soreness after the fit; (3) fit injury (tongue biting, head cut); (4) froth coming out of the mouth; and (5) falling".[20] We used the 1981 classification of seizures.[21]

2.8 | Statistical analysis

The results of the screening have been registered for each patient and entered in ad-hoc created database. Data were analyzed using STATA 16 software (College Station, TX). Data cleaning was performed before the data analysis considering both range and consistency checks. Quantitative variables were described using mean and standard deviations, while qualitative variables using percentages. Frequencies have been compared with the chi-squared test. Point-prevalence was based on the number of patients living in the study area who fulfilled the clinical diagnostic criteria proposed by ILAE[5,19] on prevalence day. Prevalence day was set at November 1, 2019. Inhabitants were only eligible if they had been resident in the communities for 6 months preceding prevalence day. Age- and sex-specific prevalence were also calculated.

2.9 | Ethics

The study has been approved by the ethics committee of the Bolivian Epilepsy Association and was conducted with the support of the Guaraní political organization (Asamblea del Pueblo Guaraní, APG). Informed consent was obtained from all the patients involved in the study.

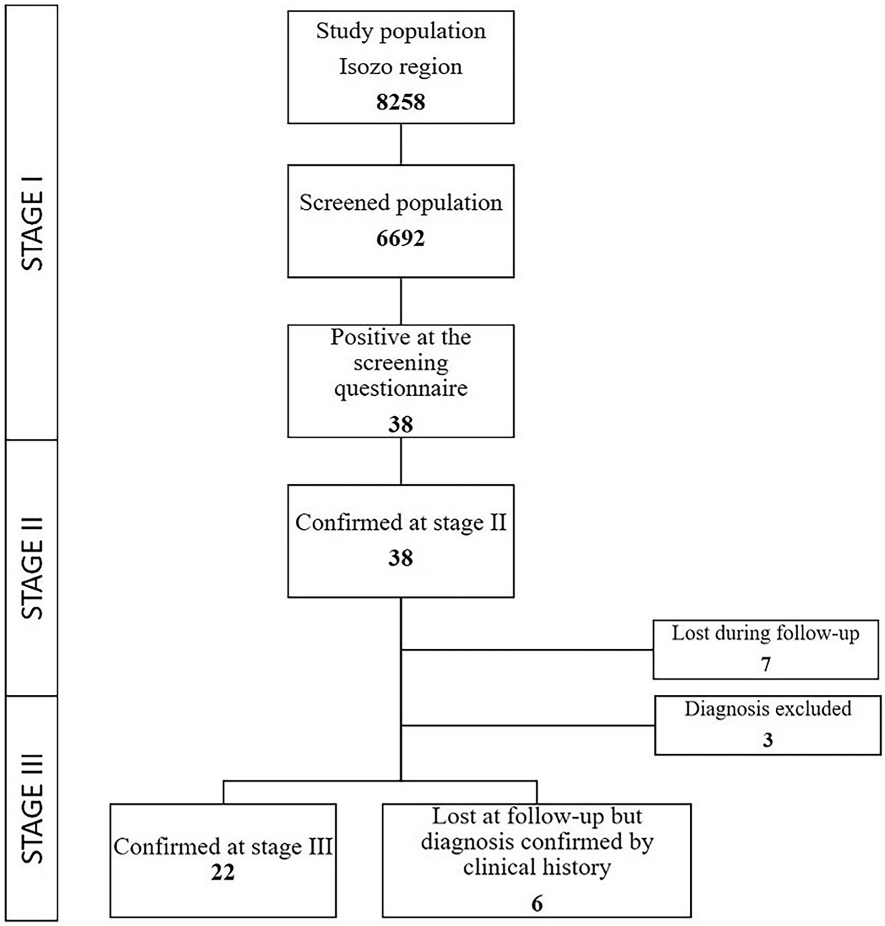
3 | RESULTS

3.1 | Prevalence

Overall, 25 rural communities of the Isozo area have been screened with a total population of 8258 people. The mean population for each community was 408.3 ± 349.14, ranging from 45 to 1358 inhabitants, with a total of 1829 families. At stage I, 1213 key informants have been interviewed, corresponding to a total screened population of 6692 inhabitants (81% of the entire population). Of them, the large majority was either the father (528; 43.5%) or the mother (483; 39.8%), while a smaller proportion was represented by the spouse (172; 14.2%) and a minority (31; 2.5%) by other family members (i.e., grandparents, brothers, or sisters).

According to the 1213 interviews performed at stage I, 38 screened positive (suspected cases) have been identified and directly interviewed at Stage II and, of them, 31 (81.6%) were also evaluated at Stage II using the Epilepsy diagnosis app. Out of these 38 positive subjects at stage II, 25 underwent a complete neurological evaluation. Of these, 22 (57.9%) were diagnosed as having epilepsy while for three subjects (7.9%) the diagnosis of epilepsy was ruled out. Six (15.8%) did not undergo a neurological evaluation because they had moved to another city between the Stage I and the Stage III, but the diagnosis was confirmed by means of clinical history recorded with a proxy and because all of them were already taking anti-seizures-medications (ASMs). Finally, seven subjects (18.4%) were lost at follow-up and the diagnosis was not confirmed at stage III. On this ground, 28 subjects were confirmed giving an overall prevalence of 4.2/1000 (95%CI 2.6–5.7) (Figure 1). Prevalence rate was similar for women and men (4.4/1000 and 4.0/1000, respectively) and steeply increased by age, reaching a peak of 7.9/1000 in the population aged 20–29 years and quickly declined soon after; a second peak

FIGURE 1 Screening flow-chart



of 5.8/1000 was recorded in the population aged 60 years and above (Table 1 and Figure 2). Considering the seizures classification, out of the 28 subjects, 21 (75%) had TC seizures, while the other seven (25%) were unknown. Of the 25 subjects fully evaluated at stage III, 12 (48.0%) were confirmed using simple videoconsultation.

It should be noted that some months after the screening and during the community awareness campaigns, 22 subjects, not identified at the screening phase, actively contacted the CHWs and the general practitioners (GPs), reporting a history of seizures. They stated that during the screening phase they denied having epilepsy due to reticence. However, after the awareness campaigns, they spontaneously sought medical attention declaring the presence of seizures. Out of these 22 subjects, for 11 (50%; 5 men and 6 women; mean age of 17.4 ± 13.2 years) the diagnosis of epilepsy was confirmed at the neurological evaluation. For four (18.2%) subjects, the diagnosis was ruled out after the neurological consultation, while seven (31.8%) moved to another area and did not undergo a neurological evaluation. Considering also these 11 confirmed cases, the overall prevalence of epilepsy in the Isozo area rose up to 5.8/1000 inhabitants (95% CI 4.0–7.7), that overlaps with the estimate obtained adjusting for sensitivity value (5.8/1000).

Concerning the 11 patients who were not identified by the screening, all presented TC seizures.

Information concerning the frequency of seizures were available for 24 cases. Except for one, 23 PWE reported at least one seizure during the past 2 years. At the time of the screening, the majority of these patients (30.4%) presented less than two seizures per week.

3.2 | Analysis of APP

Of the 25 patients who underwent a neurological examination, 20 (80%) were screened also with the Epilepsy Diagnosis App (18 with epilepsy, two with non-confirmed epilepsy). Considering the 18 PWE, the mean score was 82.1 ± 32.8. In particular, of the 18 confirmed cases, four (22.2%) presented a score lower than 80 (one had a score of 79, and the other three had a score lower than 30), leading to a sensitivity of 77.8%. Among them, three patients reported TC seizures at the time of the consultation, while one had TC seizures in the infancy with only focal seizures in the last years. The remaining two subjects for whom the diagnosis of epilepsy was not confirmed, presented a score of 10 and 22, respectively.

TABLE 1 Age- and sex-specific prevalence rates of epilepsy in the Isozo region

Age	Women				Men				Total			
	Cases	Population	Prevalence	95% CI	Cases	Population	Prevalence	95% CI	Cases	Population	Prevalence	95%CI
0–4	0	407	0	0.0	1	543	1.8	0.0–5.4	1	950	1.0	0–3.1
5–9	1	466	2.1	0.0–6.3	3	544	5.5	0.0–11.7	4	1010	4.0	0.1–7.8
10–19	5	815	6.1	0.8–11.5	6	879	6.8	1.4–12.3	11	1694	6.5	2.7–10.3
20–29	5	534	9.4	1.2–17.5	4	607	6.6	0.1–13.0	9	1141	7.9	2.8–13
30–59	1	746	1.3	0.0–4.0	0	807	0	0.0	1	1553	0.6	0.1–3.6
60+	2	202	9.9	0.0–23.5	0	142	0	0.0	2	344	5.8	0–13.9
Total	14	3170	4.4	2.1–6.7	14	3521	4.0	1.9–6.0	28	6692	4.2	2.6–5.7

Abbreviation: CI, Confidence Interval.

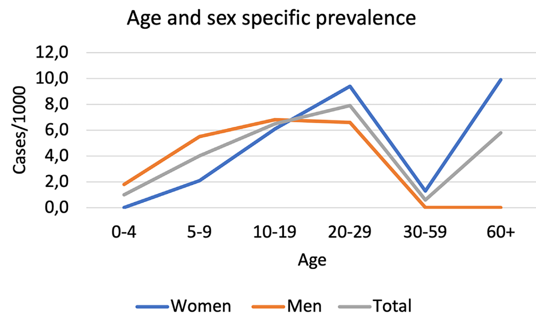


FIGURE 2 Age- and sex-specific prevalence rates of epilepsy in the Isozo region

4 | DISCUSSION

We performed a three-stage door-to-door survey to evaluate the prevalence of epilepsy with TC seizures in the Isozo area. At the end of the study, 28 people were diagnosed as having epilepsy giving an overall prevalence of 4.2/1000 (95%CI 2.6–5.7); considering other 11 subjects who were not identified by the screening, the overall prevalence of epilepsy rises up to 5.8/1000 inhabitants (95%CI 4.0–7.7). Prevalence recorded in the Isozo area was slightly lower if compared with previous studies performed in close rural areas of the Bolivian Gran Chaco.[4,22] Several factors that may explain a possible underestimation should be considered and may represent salient food for thought.

First, the present study was carried out in a "virgin" area of the Bolivian Gran Chaco, where no epilepsy related activities (training and/or awareness initiatives) have been conducted during the past 20 years, possibly explaining a greater reticence also related to the presence of stigma. Indeed, as demonstrated by previous studies, among the Guaraní population living in the rural communities of the Bolivian Gran Chaco, the lack of knowledge about epilepsy is related to high levels of stigma.[23] Educational and awareness campaigns[16,24] in these areas have been proved to be effective in improving knowledge of the population and health workers with the consequent reduction of the levels of stigma that, as well known, represents one of the main causes of ETG in this setting. This observation is also supported by the fact that during the screening phase, 22 subjects denied having history of seizures due to reticence and only after the awareness campaign performed in this area, and seeing that people treated with ASMs in the communities were feeling better, spontaneously contacted the CHWs involved in the study to undergo a neurological evaluation. For 11 of them, the diagnosis of epilepsy was confirmed. Thus, of the 39 PWE that have been identified, a significant proportion, actually the 28% have been diagnosed only after the awareness campaign. These data demonstrate once again the impact that structured interventions can have in these rural populations,

leading to greater openness to seek effective treatment. Furthermore, it should be highlighted that the Isozo area represents a very vast and remote area of the Cordillera province, hard to reach, particularly in rainy periods, where traditional medicine is particularly rooted due to cultural and economic reasons.

The innovation of this study also lies in the use of simple videoconsultation and of a validated app as a screening tool. The use of these instruments made possible to conduct the study even in the pandemic period and could represent a valuable support for epidemiological research in LMIC. Indeed the smartphone app provides a score according to which the person is considered with a high or low probability of having epilepsy and has demonstrated high levels of both sensitivity and specificity in both hospital and rural settings.[10,18] Given the widespread use of mobile phones in LMIC, this app may support the CHWs in correctly identifying PWE in their communities and its use can allow to reduce the number of false positive subjects to be confirmed by the neurological evaluation at stage III thus shortening time and costs.[17] In our study, out of the 18 PWE who were also evaluated by the Epilepsy Aid App, only four had a score below 80% (sensitivity 77.8%) while both the two unconfirmed cases had very low scores (10 and 22, respectively).

Finally, we should underline that at stage III, almost half (48%) of the screened people have been evaluated by the neurologist via a digital platform (Zoom®). Thanks to the availability of simple videoconsultation, we were able to continue the study even in a period in which movements were limited due to the pandemic lockdown. Moreover, once overcome the initial issues related to the implementation of the new procedure, the neurologist felt very confident about performing remote consultations. Indeed, the possibility to proceed with the diagnostic work-up despite anti-Covid-19 measures, together with the opportunity to avoid the long-distance travel from the city to the rural communities made simple videoconsultation the most advantageous choice. The choice of videoconsultation revealed to be very appropriate. Indeed, this instrument provides a visual feedback, that helps the clinician to conduct a virtual neurological examination and the patient to recognize a physical person that is taking care of his health, allowing the therapeutic alliance, essential for chronic diseases, particularly in settings where stigma is widespread. For this reason, videoconsultation can be considered the best option, especially for the first consultation, while telephone consultations may be used for follow-up evaluations. To the best of our knowledge, no study has been conducted to date to establish the feasibility and the usefulness of telemedicine to perform epidemiological studies on epilepsy in LMIC and further studies are needed to evaluate their possible use in future models. It is also important to underline that, regardless the epidemiological research, the approach used in our study may be in general effective to identify PWE in the remote rural communities, improving the access to care and reducing the ETG. Indeed, in rural areas of Latin American Countries, an ETG of about 80% has been estimated.[25] According to the revised conceptual definition recently proposed by the ILAE epidemiology commission,[3] ETG includes a "diagnostic gap," that is the proportion of persons in a population who fulfill the definition of epilepsy but who have not been diagnosed with epilepsy, and a "therapeutic gap," that includes the proportion of individuals with active epilepsy not receiving basic medical treatment (primary), specialist care when needed (advanced) or who require therapy but never began or are taking an inadequate dosage or discontinued taking ASMs (adherence). From this point of view all possible efforts should be made to reduce the diagnostic gap in these areas and our approach may largely contribute to this goal. We are aware that in rural settings in LMIC, despite the use of a rigorous methodology, a great effort in terms of adaptation to complex environments needs to be done. In this project, the outbreak of COVID-19 pandemic represented a further hurdle to overcome. However, the team working in the area immediately adapted to the new situation and to the use of new instruments, such as teleconsultation, to continue the project. Therefore, radical changes, especially about the use of digital supports in rural settings are feasible. Thus, we may consider the implementation of such tools in these areas with the final aim to improve the management of people with chronic diseases like epilepsy.

5 | LIMITATIONS

Our study has some important limitations mainly due to the impact of COVID-19 pandemic on the accuracy of our estimates. Indeed, although in one hand we were able to screen more than the 80% of the target population, avoiding possible selection bias and ensuring the generalizability of the results, several screened positive subjects were lost at stage III, possibly leading to an underestimation of the true prevalence. It should be noted that in the rural Chaco, seasonal migration due to job opportunities, such as for the sugar cane harvesting, are common and to this reason it is important to survey the communities at least twice, in order to reduce the number of subjects lost to follow-up. Unfortunately, due to the COVID-19 lockdown we were unable to perform all the procedures scheduled in the study protocol and to guarantee an adequate level of quality control. For instance, simple videoconsultation, not included in the original protocol, was adopted to ensure the prosecution

of the investigation without a formal validation. As a matter of fact, the use of simple videoconsultation avoided the complete failure of the survey.

6 | CONCLUSION

Although our investigation can be considered a pilot study and future studies are needed to compare simple videoconsultation vs traditional "on site" consultation for the diagnosis and follow-up of epilepsy, our experience suggests that telemedicine and the use of apps may represent a valuable aid in performing epidemiological research. Indeed, even at distance, a neurologist can confirm the presence of epilepsy, particularly in countries where the diagnosis of epilepsy remains based on clinical findings.

Thanks to the use of digital platforms, distances could be shortened improving the access to care of PWE also in the more remote rural areas with a consequent reduction of the ETG. Furthermore, telemedicine could allow patients to be followed over time facilitating the management of epilepsy treatment. Further studies in similar areas are needed in order to confirm the possible role of telemedicine also in epidemiological research.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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