CLINICAL UPDATE

Ciguatera Fish Poisoning in the Philippines: A Review of Epidemiologically-confirmed Outbreaks

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Background: Ciguatera fish poisoning (CFP) is a disease caused by the ingestion of poisonous coral reef fish. To the best of the author's knowledge, no attempt has so far been made to consolidate available reports of outbreaks in order to characterize the toxidrome of CFP in the Philippines.
Objective: To review and consolidate data from epidemiologically-documented CFP outbreaks in order to characterize the toxidrome of CFP in the Philippines and identify the areas of high risk for outbreaks.
Methods: Epidemiologic reports of CFP outbreaks in the Philippines were reviewed. A compilation of symptoms of CFP patients was done to describe the toxidrome. High risk areas in the Philippines were identified.
Results: Ten reports were retrieved related to 17 CFP outbreaks from 1988 to 2010. No epidemiologic reports were found after 2010. Consolidation of reported symptoms showed a CFP toxidrome with prominent paresthesia, muscle weakness, and myalgia with some gastrointestinal symptoms. Based on the reports, the high risk islands identified were Palawan, Panay, Romblon, the islands in the Cuyo Pass, and Basilan. Cases of CFP continue to be encountered but are not reported to public health epidemiologists.
Conclusion: When put together, the reports describe a CFP toxidrome where the neurologic symptoms predominate over the gastrointestinal symptoms. Most of the cases occurred in the west central and southern portion of the archipelago suggesting a higher risk for CFP in that area. Cases of what appear to be CFP continue to be diagnosed although they are not reported to government epidemiology units. More systematic surveillance of CFP by government agencies is needed.

Keywords: Ciguatera fish poisoning, Philippines, Coral reef fish

Introduction

Ciguatera fish poisoning (CFP) is a disease caused by the ingestion of poisonous coral reef fish. CFP occurs mainly in the Pacific Ocean, the Caribbean basin and the Indian Ocean.[1,2,3] The poisonous fish contain ciguatoxin congeners (CTX), synthesized by the dinoflagellate *Gambierdiscus toxicus*. The poisonous fish are typically the larger carnivorous ones, reflecting the bioaccumulation of CTX as one goes up the food chain.

The toxidrome of CFP is gastroenteritis with prominent neurologic manifestations such as paresthesia, dysesthesia, pruritus, allodynia (hot-cold sensory reversal), myalgia, arthralgia, and dizziness. Bradycardia and hypotension may also occur although are less frequent.[4]

Disturbances in the reef resulting in dead coral are usually the first events leading to CFP outbreaks. The Philippines has an extensive system of coral reefs but destructive fishing practices, sedimentation and pollution from land-based sources, and supertyphoons like Typhoon Haiyan have led to the death of many corals,[5,6,7] making the Philippines fertile ground for CFP outbreaks. The risk may be further aggravated by higher sea surface temperatures which have risen from 1985 to 2006 by 0.3 and 0.2 degrees Celsius per decade in the northern and southern part of the Philippines, respectively.[8] Such increases in sea surface temperatures have been shown to cause coral death[6,9,10] and increased populations of Gambierdiscus species.[11,12]

The number of people who suffer from CFP annually range from 25,000 to 50,000 worldwide but due to under-reporting of cases, these probably represent only 10-20% of actual CFP cases.[4] In the Philippines, CFP is a largely unknown entity among doctors and it is reasonable to assume that the problem of under-reporting is also present in the country. Although there are epidemiologic reports of CFP outbreaks in the country, these reports have not been consolidated so as to form a clearer picture of this disease entity. Hence, the objective of this paper was to review and consolidate the documented CFP outbreaks in order to characterize the toxidrome of CFP, identify the areas of high risk for outbreaks, and propose recommendations for surveillance control in the high risk areas.

Methods

This was a descriptive study reviewing epidemiologic reports of Philippine CFP outbreaks. Records of such reports were gathered from the library of the National Epidemiology Center of the Department of Health (DOH) Philippines using their online public access catalogue.[12]

In addition, a search of Philippine online news reports using Google was done using the search terms "*fish poisoning*" and "*ciguatera*." A search was also done for journal articles that made mention of CFP outbreaks in the Philippines using the Herdin NeoN database, the Philippine Health Research Registry, Researchgate and MEDLINE. Inquiries were also made to all Regional Epidemiology and Surveillance Units (RESU) of the DOH to find out if epidemiologic reports existed that documenting any CFP outbreaks in their respective regions. Feedback was obtained from all the regions except for Bicol (Region 5) which, as of this writing, is still pending. Inquiries were also made from the Bureau of Fisheries and Aquatic Resources (BFAR) for any CFP-related data.

The lead persons of the following offices were also interviewed for further data related to Philippine CFP outbreaks: the Region 6 RESU, the Aquatic Toxicology Laboratory of the BFAR, and the poison centers of the Zamboanga City Medical Center, the Corazon Locsin Montelibano Memorial Regional Hospital in Bacolod, and the East Visayas Regional Medical Center in Tacloban. The attending doctor of 18 patients in a possible CFP outbreak in Zamboanga was also interviewed.

Only outbreaks that were confirmed by an epidemiologist or by laboratory identification of CTX in the offending fish or in biologic samples from the patients were included in this review. In addition, only outbreaks that involved fish caught in Philippine waters, and only outbreaks that were associated with fish known to produce CFP were included. From the collected reports, the circumstances surrounding the outbreaks were collated narratively. The signs and symptoms from the reports were collated numerically and, when appropriate, proportions and frequencies where used to summarize the data.

Results

A total of 10 documents detailing 17 confirmed outbreaks were included in the review, the details of which are in Table 1. One outbreak was in Basilan[13] , 1 in Navotas, Metro Manila,[14,15,16] 11 in Sibuyan Island, Romblon,[17] and 4 in the province of Iloilo.[3,18,19,20,21] It should be mentioned that in the Sibuyan report, apart from the 11 outbreaks mentioned above, there were two-outbreaks one involving anchovies "dilis" and another

involving parrotfish that did not appear to be CFP. Anchovies are not typically associated with CFP, hence the non-inclusion of this outbreak. The two fatalities and 3 of the 5 hospitalizations recorded in the original report were from the parrotfish outbreak, but while parrotfish are associated with CFP, the manifestations of the patients (board-like rigidity of the abdomen and tetanus-like posturing) were more consistent with palytoxin rather than ciguatoxin, hence its non-inclusion in this paper.

There was a report of a French tourist who contracted CFP from the Philippines. His case was included in a review of 18 French tourists who contracted CFP outside France

Table 1. Details of epidemiologically confirmed CFP outbreaks in the Philippines (1989 to 2018).

Confirmed Outbreaks	Reference	Number of Patients	Age Range In Years	Hospitalized Patients	Fish Involved	Origin of Fish
Basilan, August 1988	Guerrero 1989[13]	19 (11F, 8M) (4 households)	4 to 61 (mean 26)	Hospitalizations occurred but number not reported.	*Syphraena jello*	Caught "in the vicinity of Basilan"
Sibuyan Island, Romblon, September 1, 1997 to February 12, 1998	Castillo, et al. 1998[17]	25 (11 incidents involving different fish)(male/female distribution not available) (number of households not available)	6 to 70 (median 28)	2	*Lethrinus sp* *Gymnocranius sp* *Pagellus sp* *Lutjanus sp*	caught in the vicinity of Sibuyan Island
Navotas, Metro Manila June 6, 2001	Tante, et al. 2001a[14] Tante, et al. 2001b[15] Tante-Apurillo, et al. 2002[16]	38 (22F, 16M) (number of households not described)	2 to 68 (median 36)	3	*Sphyraenidae sp.*	source of fish traced to Palawan
Oton, Iloilo, June 2005	Alonsabe and Gallardo 2006a[18]	No data	No data	No data	*Lutjanus bohar.*	No data
Oton, Iloilo, June 7, 2006	Alonsabe and Gallardo 2006a[18]	7 (4F, 3M) (1 household)	10 to 51 (no mean or median reported)	4	*Lutjanus bohar.*	No data
Iloilo City, August 6, 2006	Alonsabe and Gallardo 2006b[19] Michille 2006[20]	35 (25F, 10M) (8 households)	2 to 65 (median 32)	34	*Sphyraenidae sp.*	Cuyo Pass, northern Sulu Sea
Mina, Iloilo, June 21, 2010	Mendoza, et al. 2013[3] Ponsaran-Rendon 2010[21]	22 (2 households)	1 to 50 (no mean or median reported)	22	*Lutjanus campechanus*	No data

and who consulted in a French poison center[22] but no other details about the case were given so this was not included. A report was found about 5 Filipino seafarers who contracted CFP after eating barracuda when they were docked in the Caribbean.[23] Since the barracuda did not come from Philippine waters, this case series was not included. Finally, an online news report was retrieved that describing how 18 construction workers in Zamboanga became ill after eating barracuda.[24] Although CFP was highly suspected by the attending physician, no epidemiology report could be found confirming the diagnosis and the outbreak was not included.[25]

Description of the Outbreaks

1. Basilan Island, August 1988

The first ever recorded outbreak of CFP was in August 1988 in Basilan Island involving 19 persons from 4 households, aged 4 to 61 years, after eating a single barracuda (*Syphraena jello*).[13] Some patients were hospitalized but the report did not indicate how many. The fish was caught in the vicinity of the island and CTX at levels > 3ng/g (or >3 ppb) was detected in the cooked meat of the fish using a stick enzyme immunoassay method. Mild symptoms can already appear after eating fish containing 0.1ppb of Pacific CTX.[26]

2. Sibuyan Island, Romblon, September 1997 to February 1998

Between September 1, 1997 to February 12, 1998. 11 incidents of CFP involving 25 persons, aged 6 to 70 years, took place in Sibuyan Island, Romblon.[17] Two were hospitalized. The fish involved were *Lethrinus sp* ("manambuyao" or "dugso", English common name "emperor") in 7 outbreaks, *Gymnocranius sp*. ("dayang dayang", English common name "emperor") in 2 outbreaks, *Pagellus sp* ("isdang bato", English common name "porgy") in 1 outbreak, and *Lutjanus sp* ("ahaan", English common name "snapper") in another. All of the fish were at least 3kg in size. All the fish were caught in the vicinity of the island. The presence of CTX, however, was not documented and the diagnoses were based on clinical features.

3. Navotas, Metro Manila, June 2001

A third report described the outbreak of CFP in Navotas, Metro Manila on June 6, 2001[14,15] involving 38 patients ranging from 2 to 68 years of age. Twenty-two sought medical consultation and 3 were hospitalized. They all ate from one batch of barracuda (*Sphyraenidae sp*.) purchased from a single vendor. Samples of fish liver from the batch were tested using a membrane immunobead assay method and the samples showed CTX levels of of 2-3ppb.

In order to trace the origin of the fish, the BFAR randomly sampled fish from different regional fish markets and the results pointed to Palawan as the source. The report stated that *Gambierdiscus toxicus* was subsequently found in the fishing grounds, that fish samples from the area were positive for CTX, and that harvesting of reef fish from waters with ciguatoxic fish was subsequently prohibited. The report, however, did not state what fishing grounds were involved.[16] While the original BFAR report on CTX in the fish samples is not available, in an interview for this paper, the head of BFAR's Aquatic Toxicology Laboratory, who did the testing of fish, confirmed that the Palawan specimens were positive for CTX.[27]

The report also stated that after the Navotas outbreak, CFP case surveillance resulted in the identification of 19 additional CFP cases "from various areas", between June 2001 and June 2002[16] but these "areas" were not identified and no further details about the cases were given, so these cases were not included in this review.

4. Oton, Iloilo June 2005 and June 2006

Two outbreaks, one year apart, occurred in Oton, Iloilo which is a coastal town 11 km west of Iloilo City. On June 7, 2006, there was an outbreak involving 7 patients, ages ranging from 10 to 51 years old, who had ingested "maya-maya", also known as "bagangan" (English common name

"snapper"). All sought medical consultation and 4 were hospitalized.[18] Fish samples were sent to the BFAR for CTX analysis. An inquiry with BFAR, however, revealed that the records for that time period were unavailable.

The report went on to state that: "The RESU record showed that ciguatera fish poisoning occurred in Oton exactly a year ago. The fish was identified as *Lutjanus bohar* or 'red snapper' …commonly known as 'maya-maya' or 'bagangan'." The 2005 report could not be found, but since the outbreak had been investigated by the same authors of the 2006 report, and because clear reference was made to the report's existence, the 2005 outbreak was considered as a confirmed CFP outbreak.

5. Iloilo City, August 2006

An outbreak involving 35 patients from 8 households, ages ranging from 2 to 65 years of age, took place in Iloilo City on August 6, 2006, one month after the outbreak in Oton. Of the 35 patients, 34 were hospitalized.[19] The fish involved was barracuda purchased from a single fish vendor in the Villa Arevalo public market. Fish samples were sent to the BFAR but the records of the tests were unavailable. However, a news report about the outbreak quoted a BFAR report which stated that "...barracuda fished from Cuyo Pass and landed in Barangay Butuan, Anini-y, Antique were found to be positive for ciguatoxin," and the public was warned not to eat barracuda caught in the Cuyo Pass.[20] In an interview for this paper, the head of the BFAR Aquatic Toxicology Laboratory confirmed that he did the testing for these specimens and that the test was positive.[27]

6. Mina, Iloilo, June 2010

Mina is a town about 30 km north of the port of Iloilo City. There was a RESU report of the outbreak but it could not be found. However, a news report[21] and a journal article[3] about the outbreak were available. On June 21, 2010, 22 individuals from 2 households, ages ranging from 1 to 50 years, were diagnosed to have CFP. All were hospitalized. The fish involved was "maya-maya" (English common name "snapper") later on identified as *Lutjanus campechanus*. CTX determination in the available remaining fish meat was positive using an enzyme-linked immunosorbent assay method. Blood samples from some of the patients revealed the presence of CTX-1 and CTX-3B/3C.[3]

In summary, documents describing 17 confirmed CFP outbreaks involving at least 146 patients were gathered, 11 in Sibuyan, 4 in Iloilo province, 1 in Basilan, and one in Navotas Metro Manila. Except for Navotas, the locations of the outbreaks described above were in the western central and southern Philippines: the Cuyo Pass between Palawan and Panay and the islands of Panay, Sibuyan, Palawan and Basilan. Even the Navotas outbreak was traced to a fishing ground in Palawan. The outbreaks were usually associated with a family meal, and the usual trigger for reporting the outbreaks to the authorities was hospitalization of several family members after ingesting the poisonous fish.

Signs and Symptoms of CFP

In the outbreak reports of Basilan,[13] Sibuyan,[17] Navotas[14,15,16] and Mina,[3] symptoms were recorded and frequencies obtained. The combined symptoms and their frequencies are listed in Table 2. There was wide variability in the manner the symptoms were listed in original reports, so some aggregation of similar symptoms was done to facilitate tabulation. Symptoms less than 15% were not included in the table.

The most frequently encountered neurologic symptoms were paresthesia of the distal extremities (66.3%), weakness of extremities (52.9%), myalgia (26.9%), and hot-cold sensory reversal (25%). Gastrointestinal symptoms encountered were abdominal cramps (48.1%), diarrhea (38.5%) and vomiting (30.8%). There was no mention of bradycardia or hypotension in the reports.

Three reports (Basilan, Sibuyan, and Navotas) described incubation periods albeit in different ways. The Basilan report described the range as 1 to 12 hours with a mean of 6 hours and a standard deviation of 2.73. The report about Sibuyan described the incubation period as a range (4 to 28 hours) and as intervals--5 cases had incubation periods of

Table 2. Frequency of symptoms in 4 outbreaks of CFP in the Philippines.

	Basilan 1988[16]	Sibuyan, Romblon 1997[18]	Navotas, Metro Manila 2001[19,20,21]	Mina, Iloilo 2010[3]	Total	Percentage
Number	19	25	38	22	104	100.0
Neurologic						
Paresthesia of the distal extemities	14	17	36	2	69	66.3
Weakness of extremities	14	22	16	3	55	52.9
Myalgia	14	8	6		28	26.9
Hot cold sensory reversal	11	2	12	1	26	25.0
Perioral paresthesia		4	15		19	18.3
Ataxia	11	5			16	15.4
"stiffness of extremities and difficulty in opening mouth" *	16				16	15.4
Gastrointestinal						
Abdominal cramps	6	6	25	13	50	48.1
Diarrhea	1	11	22	6	40	38.5
Vomiting	2	5	15	10	32	30.8
Miscellaneous						
Dry lips and/or buccal mucosa				21	21	20.2
Joint pains	14	3			17	16.3

*quoted from Guerrero 1989[13]

less than 10 hours, for 10 cases the period was 10-20 hours, and for 7 cases, the period was more than 20 hours. No data was available for 3 cases. The Navotas report described a range of 1-24 hours with a median of 6 hours.

Only the Sibuyan report had data regarding the duration of the symptoms of the CFP patients post-ingestion. Nine had symptoms for less than a week. Thirteen patients had symptoms for 1 to 2 weeks. One had symptoms for 1 month and another had symptoms that persisted for 4.5 months. There was no data for one patient.

This paper's objective is to describe the toxidrome of CFP in the Philippines. In summary, based on the frequency of symptoms, the emerging CFP toxidrome appears to be one which is primarily neurologic and secondarily gastrointestinal. Paresthesias and weakness of the extremities (66.3% and 52.9% respectively) are a prominent feature and are even more frequent than the gastrointestinal manifestations of abdominal cramps (48.1%), diarrhea (38.5%) and vomiting (30.8%). Hypotension and bradycardia, were not among the symptoms listed in the reports.

The other objective of the paper was to identify areas with increased risk of CFP. It appears that west central and southern Philippines, specifically Palawan, Panay, Sibuyan, Basilan, and the Cuyo Pass are the areas of higher risk.

Discussion

1. Philippine CFP toxidrome compared to descriptions in the international literature

The predominance of neurologic symptoms in Philippine CFP is consistent with the observation that in the Caribbean, gastrointestinal symptoms predominate whereas in the Pacific, neurologic symptoms are more

prominent. This can be explained by the fact that Pacific CTX congeners, cause more prolonged opening of voltage-gated sodium channels and are 10-fold more toxic relative to Caribbean CTX congeners.[3,28]

The wide range of incubation periods in this case series is consistent with the observations in other countries that gastrointestinal symptoms can occur within up to 12 hours from the ingestion of toxic fish and neurologic symptoms can appear up to 48 hours post-ingestion.[4]

Fifteen patients in the Sibuyan outbreak had prolonged symptoms, one of them lasting for one month and the other lasting for 4.5 months. This is consistent with the observation in other countries that peripheral neurologic and systemic symptoms may persist for weeks or months.[3,29] Exposure to fish, caffeine, nuts, chicken, pork and physical overexertion or dehydration can precipitate a recurrence of the symptoms. The hypotheses that have been proposed for these recurrences include cross-sensitization to CTX as well as possible mobilization of CTX from fatty tissue.[4]

All of the fish involved in the reports were big predatory fish. This is consistent with the phenomenon of bioaccumulation that has been described in CFP where the toxin load in the organism increases as one goes up the food chain.[4,29]

In most of the reports in this review, the poisonings took place in the setting of households sharing a meal of toxic fish, which accounts for the wide range of ages of patients affected, from children to the elderly.

The outbreaks in this review came to the attention of public health authorities only when there were hospitalizations. Based on international experience, only 20% of cases are reported to health authorities.[1,4,32] It is conceivable that there are significantly more CFP cases in the Philippines that similarly go unreported because no hospitalization is needed. It is also probable that the diagnosis of CFP can be missed by physicians in the front line because of unfamiliarity with the disease entity.

There were no deaths in this review of cases. The absence of fatalities in this series is consistent with the literature which states that CFP is rarely fatal.[4]

2. Temporal synchronicity of the outbreaks

Gambierdiscus spp. thrive in higher water temperature.[11,31] Furthermore, in French Polynesia, it was demonstrated that there is a lag time of approximately 3 months between peak densities of *Gambierdiscus polynesiensis* and CFP outbreaks.[32] The hot dry season in the Philippines is from March to May.[33] The outbreaks in Navotas, Oton in 2005, Oton in 2006 and Mina took place in June while the Basilan and Iloilo City outbreaks occurred in August, one month and 3 months respectively after the end of the hot dry season. It is possible that blooms of *Gambierdiscus sp*. occurred during the hot dry months followed by outbreaks within 3 months from the blooms.

The Sibuyan data showing 11 outbreaks over 6 months starting September does not follow the same pattern and suggests a continuing presence of dinoflagellates and ciguatoxic fish in the area independent of season.

3. Explanation for the absence of confirmed CFP outbreaks since 2010.

It is notable that there have been no RESU reports of confirmed CFP outbreaks from the high risk islands since 2010. Inquiries with the RESUs of Region 4B (covering Mindoro, Masbate, Romblon, and Palawan), Region 6 (Western Visayas), Region 9 (Western Mindano), and Region 7 (Cebu) were done and no reports have been received over the last 8 years. This is probably because, at the moment, only passive surveillance of CFP is being done by the different RESUs in the high risk areas. Active investigation takes place only when there are hospitalizations. Except for the post-Navotas outbreak surveillance, where an additional 19 CFP cases were found, the reports in this review did not indicate that continuing active surveillance was done post-outbreak. As previously mentioned, world-wide, only 20% of CFP cases are reported to public health authorities[4] and the same phenomenon is probably happening in the Philippines.

There is evidence, however, that CFP cases continue to occur. Clinical toxicologists based in Bacolod, Zamboanga, and Tacloban have informed the author that they have

handled a combined total of 9 cases of CFP since 2015. The head of RESU 6 in Iloilo City also told the author that he would hear about 1 or 2 cases of CFP every year that would not be formally reported to the RESU (unpublished data). In the previously mentioned 2014 Zamboanga outbreak of fish poisoning involving 18 patients who had eaten barracuda, the attending physician of the patients said that her primary diagnosis was CFP but there was no epidemiologic investigation that was done to confirm her diagnosis.[25]

Limitations of the Study

True prevalence of CFP in the Philippines cannot be determined from the reports in this paper. Only outbreaks that were reported to the epidemiologists of the affected regions were included, and in only one report was active post-outbreak surveillance done though it was not sustained. It is probable that many more cases go unreported in the entire archipelago.

The data presented in this paper are also limited by the variations between reports in the manner in which symptoms were recorded. In addition, records of CTX testing were not available for most of the outbreaks, although many of the reports clearly stated that specimens had been sent to BFAR for this purpose.

Conclusions and Recommendations

The toxidrome emerging from the consolidated data of the outbreaks reviewed demonstrate a clinical entity manifesting primarily with neurologic symptoms (paresthesias and weakness of the extremities, myalgia, and hot-cold sensory reversal) and secondarily with gastrointestinal symptoms (abdominal pain, diarrhea, and vomiting). The manifestations are consistent with that described for Pacific CTX congeners. The pattern of outbreaks suggests a high risk area in the islands of Palawan, the Cuyo Pass, Sibuyan, Panay and Basilan in west central and southern Philippines. There are continuing reports of fish poisoning outbreaks compatible with the diagnosis of CFP, and it is probable that most cases go unreported.

Given the already degraded condition of Philippine coral reefs and the further degradation that could come as a result of climate change, more cases of CFP can be expected. More systematic case finding and surveillance should be done by public health authorities. An effort needs to be made to educate doctors, especially those in the coastal areas, about CFP and to encourage them to report suspected cases. Coordination with BFAR can identify the high risk reefs so that reasonable control measures to protect the public and the fishing industry can then be instituted.

Acknowledgements

The author would like to acknowledge the assistance of the following individuals who greatly assisted in the writing of this article: Dr. Marc Lawrence J. Romero, section chief of the National Fisheries Laboratory Division, BFAR; Dr. Jesse Glen L. Alonsabe, head of the Region 6 RESU, Dr. Eunice Sapaap, attending physician of the Labuan District Hospital, Zamboanga City; Dr. Aeesha Yahcob-Pingli, clinical toxicologist of the Zamboanga City Medical Center; Dr. Cherie Grace Quingking, clinical toxicologist of the Corazon Locsin Montelibano Memorial Regional Hospital in Bacolod; Dr. Lourdes Agosto, clinical toxicologist of the East Visayas Regional Medical Center in Tacloban.

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