

# FAMILIAL CLUSTERING OF PRESUMPTIVE SUDDEN UNEXPLAINED DEATH SYNDROME (PSUDS)

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**Abstract.** Regarding the suggestion that presumptive sudden unexplained death syndrome (PSUDS) may be genetically associated, we recently conducted a study to reveal the clustering of the PSUDS in extended families. The data collection was done through case searching, interviewing using structured questionnaires and cross-referencing among informants. The precise criteria were used to identify the SUNDS cases. The collected data were age, sex, time and place of death, details of events at death, and vital statistics of relatives. There were forty-nine families with 418 family members included in the study. Twenty-five cases of PSUDS were reported from 14 families. All were men, with the mean age ( $\pm$  SD) 31.26 ( $\pm$  7.01) years and the age range was 25-50. There were 6 clusters of SUNDS in sibling groups. Three of the clusters consisted of three siblings each and the other three clusters consisted of two siblings each. Most of the individuals in the siblings clusters had different occupations and died in different places and in different years. The aggregation of PSUDS in families is demonstrated. However, whether it is genetically related needs further study.

## INTRODUCTION

Recently sudden unexplained death syndrome (SUDS) has caught the public's attention in Thailand after it has been known to exist locally for many decades without any official record. The mysterious deaths among Thai workers in Singapore (Goh, 1990) have aroused political and public concerns about SUDS. The syndrome is characterized by sudden death of healthy young adults, mostly male, occurring in their sleep. It may be preceded by agonal respiration, agitated movement and sleep from which it is difficult to awaken them.

The syndrome has been reported to have afflicted mainly Southeast Asian ethnic groups and Japanese (Parrish *et al*, 1987; Sugai, 1959). The incidence among Hmong refugee males in the USA, age 22-44 years, was reported to be about 90 per 100,000 per year (Parrish *et al*, 1987). It is roughly estimated to be about 70/100,000/year among Thai males age 20-49 years (Tatnavivat *et al*, 1990).

Reported necropsy results (Cruz, 1952; Sugai, 1959; Parrish *et al*, 1987; Goh *et al*, 1990) are unable to definitively identify the pathophysiological

mechanism responsible for the fatal event. The case-control study which was done by Goh *et al*, (1990) among Thai workers in Singapore suggested that there were similar deaths among family members of the victims. Also Munger (1987) showed in his study among Southeast Asian refugees in Thailand that SUDS occurred among relatives of the cases while none were found among the controls.

Therefore, we conducted a family-tree study on presumptive SUDS (PSUDS). The SUDS is presumptive because necropsy was not performed according to the criteria suggested by the SUNDS Planning Project (Holton *et al*, 1984). The purpose of the study is to present the evidence for family aggregation of the syndrome.

## CASE REPORTS

### Propositus 1

The first case was a 35 year old Thai male who worked as a company employee. His family was in Khon Kaen. He went to Chiang Mai to work and was found dead in his sleep the night before the scheduled early morning arrival of his visiting

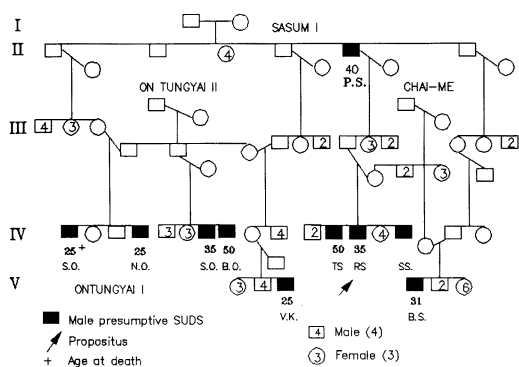


Fig 1—A family tree to demonstrate PSUDS in the first extended family with 3 clusters of PSUDS in siblings.

wife. He had been working regularly without any complaint before the fatal event. As reported by his friends, he was very happy that night anticipating the arrival of his wife. Interviewing his family revealed that two of his brothers, his grandfather and one of his maternal cousins also died in their sleep in different years at the ages of 50, 25, 40 and 31, respectively. Extensive interviewing among his relatives showed that there were 5 additional cases in the extended family tree, one of whom died while taking a daytime nap. (Fig 1)

**Propositus 2**

A 35 year old Thai, a merchant, came to see a physician and requested an extensive workup after he had heard the news of SUDS in the newspaper and on television. He reported that the characteristics of SUDS as reported by the news were similar

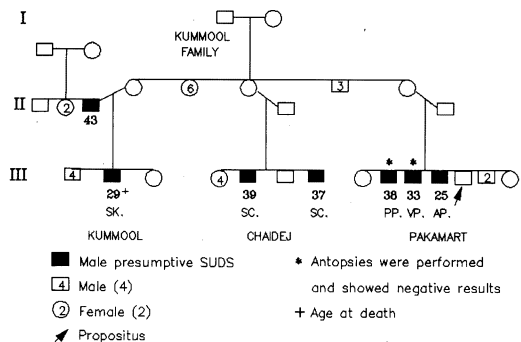


Fig 2—A family tree of the second extended family with 2 clusters of PSUDS in siblings.

to what had happened to his three brothers. Of course, he appeared to be healthy after the physical check up. Further interviews in the extended family, through his mother's sibling, showed two clusters of presumptive SUDS in sibling groups. In one sibling group, two out of three brothers died, and in another sibling group three out of six brothers dies (Fig 2). Two of these brothers eventually had postmortem examinations by the same qualified pathologist at the provincial hospital and showed no significant findings.

**MATERIALS AND METHODS**

The study area was within the vicinity of Khon Kaen Province, situated in the center of the north-eastern part of Thailand. The study populations were in three geographically separate villages. These were Nongkoy village in Tar Phra subdistrict, Bueng niium village in Bueng niium subdistrict, and Nong Bua Kummoool village in Ban Non subdistrict. The first two villages were less than 20 kilometers and the last one was about 40 kilometers from Khon Kaen.

**Study case definition.**

Presumptive SUDS : for a witnessed case, the victim must have at least 4 and for a non-witnessed case, the victim must have at least 3 of the following criteria :

1. The victim must be 20-50 years of age.
2. The event occurs during sleep or a short nap.
3. The victim is known to be healthy until immediately before the event takes place.
4. There is agonal respiration or difficulty in breathing before death.
5. Awaking is difficult or unsuccessful.
6. No necropsy is performed.

**Case finding**

From extensive interview with the families of the propositi, as well as the village headmen, we were informed of many more death-during-sleep cases in the same village. Accordingly, we carried out extensive interviews for every family which was verbally reported to have such deaths occurring in the family. Structured questionnaires were used for every interview. When an additional case was identified and adhered to the study case definition,

cross-referencing interviews were conducted with several members of the family as well as the neighbors and the village headmen.

**Data collection**

The variables were: demographic data; details of the events, eg age of the victim, time, date, and place of events, manifestations at the moment before death; number of family members and relatives; the vital statistics of the relatives of the deceased. Data collection was done by interviewing the close relatives of the victims; most of the time, there were both parents and siblings around to provide details. Family trees were drawn and details were verified again.

**RESULTS**

Forty nine family trees were collected with 418 members, all were ethnic Thai (Table 1). There were 223 males and 195 females. The first case in this series was reported to have take place in 1971. Twenty five cases of presumptive SUDS were reported from 14 families. There were 5 nonclustered cases that had occurred in 5 different families.

Nine of the fourteen families could be connected together in three extended families, which had 20 PSUDS cases (Fig 1-3). Among them were 6 clusters of PSUDS in sibling groups. Three of the clusters consisted of three siblings each and the other three clusters consisted of two siblings each. The majority of the cases died in their homes. However, most of the individuals in the sibling clusters had different occupations and died in

Table 1

Results of interviews of family members.

Interviewees	27
Sibships	49
Family members + PSUDS	418
Male : Female	1.1 : 1
Number of families with PSUDS	14
Number of PSUDS (all male)	25
Mean age (SD) (Years)	31.26 (7.01)
Age range (Years)	25-50
First reported case in	1971

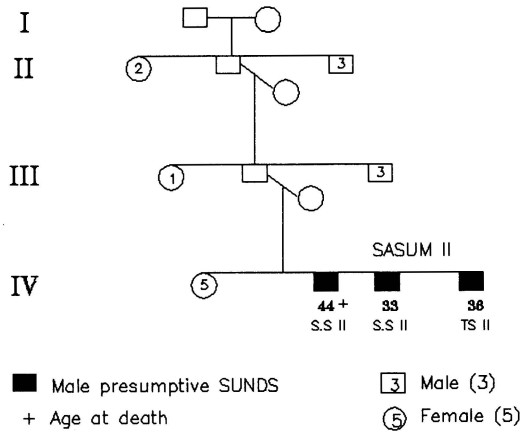


Fig 3—A family tree of the third extended family with a cluster of PSUDS in siblings.

different places and in different years (Table 2). In addition, the study showed that most of the victims developed PSUDS during the period of March to April with the time span ranging from November to June. All were men, the mean age ( $\pm$  SD) was 31.26 ( $\pm$  7.01) years and the age range was 25-50.

**DISCUSSION**

We are aware that the method of case finding through verbal reports used in this study may have a higher chance of detecting PSUDS in clusters than in isolated cases, because people tend to recall repeated events more easily. Thus in addition to data obtained from interviewing families, we also asked any available villagers who came to join our ongoing conversation with the family with PSUDS to find any other such case in the village. However, since we intend to show the familial clustering of PSUDS instead of the proportion of isolated cases compared to familial clustering, underreporting of the isolated cases should not cause any problem.

A retrospective study has the inherent weakness of recalled data. It is even more so when dealing with sudden death without coronial examination. However the sudden unexplained death syndrome appear to be quite striking in its characteristics. From personal communication with Professor Chao Tzee Cheng, Director of the Institute of Science and Forensic Medicine, Singapore who has done necropsies on hundreds of Thai workers

Table 2

Details of PSUDS in sibling groups at the time of death.\*

		Age	Place of event	Occupation	Month	Year
Pakkamart	PP	38	Bueng Niem Village	Teacher	March	1989
	VP	33	Ta Phra	Foreman	March	1986
	AP	25	Sukothai	Teacher	March	1983
Chaidej	SC	39	Bueng Niem	Farmer	November	1988
	SC	37	Nong Bua Kummoool	Farmer	December	1986
Sasum I	TS	50	Ban Neng	Teacher	January	1985
	RS	35	Chiang Mai	Foreman	April	1990
	SS	25	Nongkoy	Company worker	November	1976
Sasum II	SS II	44	Nongkoy	Farmer	April	1979
	SS II	36	Nongkoy	Farmer	March	1981
	TS II	33	Nongkoy	Worker	March	1983
Ontungyai I	S O	25	Nongkoy	Farmer	April	1977
	N O	25	Ta Phra	Worker	April	1987
Ontungyai II	S O	35	Nongkoy	Farmer	—	1976
	B O	50	Nongkoy	Farmer	January	1990

\* Another 10 PSUDS were not shown because they were not PSUDS death in sibships.

in Singapore, including the SUDS cases, since 1981, we have learned that among those who had explainable causes of death, none had the following characteristics in combination: being healthy, death occurring during sleep or while at rest, having breathing difficulty and being difficult to awaken from sleep. Therefore, using these characteristics as the strict case definition and for cross-referencing in this study may overcome the weakness of the study concerning the potential of recruiting non-SUDS victims into the study. In addition, negative autopsy results were found in postmortem examination on two of the reported PSUDS victims in this study (Fig 2).

This is probably the first extensive family tree study on PSUDS. Although several studies (Goh *et al*, 1990; Munger, 1987; Lemoine and Mougne, 1983) have shown family aggregation, the information regarding SUDS in families in the study by Goh was given by friends of the victims which could be less than accurate and would be difficult, if not impossible, to confirm by the cross-referencing method. Munger had obtained the information among relatives of victims in refugee camps in Thailand; however, the study had some limitations,

because among refugees, families were fragmented and some of the information might have been lacking simply because fewer family members were available for interviewing. This could also be the case in the report of Lemoine and Mougne.

Though the information is less than adequate to suggest a pattern of inheritance of PSUDS, when considering the differences in years of death, places and occupations among the sibling victims, immediate environmental factors can have less explanatory power as the attributable causes. However, these sibling victims shared the same family environments for many years while they were young, so they might have acquired the same environmentally-related risk factors. These risk factors could possibly predispose them to be vulnerable to precipitating factors such as stress, and lead to untimely death later. In addition, the lack of any evidence in these families of female victims, who shared the same domestic environment with the men, could lessen the environmental explanation of PSUDS. The afflicted men in the Kummoool kindred were related to one another through females (Fig 3), which could possibly suggest a sex-linked recessive pattern of inheritance,

but such a relationship was not demonstrated in the other families.

In addition, the deaths of father and son in the Kumool family might also contradict the sex-linked recessive criteria but in this particular family both parents had the same last name of Kumool. Whether both were from the same ancestor or not was not definite.

Therefore, the aggregation of PSUDS in families is definitely demonstrated, but whether it is genetically-related needs further study to confirm and to separate the environmental factors from genetic ones.

#### ACKNOWLEDGEMENTS

The authors are grateful of the office of Research Affairs of the Dean of the Faculty of Medicine, Khon Kaen University, and the Royal College of Physicians of Thailand for funding and technical support. We are also grateful to Professor Vicharn Panich and Associate Professor Chintana Sirinavin for their advice, and to Professor Chao Tzee Cheng, Director of the Institute of Science and Forensic Medicine, Singapore, for his kind correspondence to us of the results of autopsies of Thai workers in Singapore. We would like to thank Miss Upatham Mahachokchai and Mr Somyot Duangrudeesawat and Mr David Narot for assistance in manuscript preparation.

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