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The Southern House Mosquito, *Culex quinquefasciatus*: profile of a smart vector

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Abstract

Culex quinquefasciatus is the principal vector of bancroftian filariasis and a potential vector of *Dirofilaria immitis.* This mosquito species is also a potential vector of several arboviruses like West Nile virus (WNV), Rift Valley fever virus, avian pox and protozoa like *Plasmodium relictum* that causes bird malaria. This species has the ability to transmit other nematodes like *Saurofilaria sp.*, *Oswaldofilaria sp.* In the USA, it is a potential vector of St. Louis encephalitis virus (SLEV). Japanese encephalitis virus (JEV) has been isolated from this mosquito in several occasions in Asia. Furthermore, it can transmit several other arboviruses in the laboratory conditions. This article is an attempt to review the bio-ecology, medical and veterinary importance of *Culex quinquefasciatus.* It acts as an important "urban bridge vector" which bridges different reservoir/amplifier hosts to humans because of its encounter with different vertebrates. *Culex quinquefasciatus* also creates an ecological bridge between urban, periurban and rural areas owing to its presence and adaptability in diverse ecological niches. *Culex quinquefasciatus* emerged as a smart vector because of the adaptive fitness, ecological plasticity, invasive behaviour, host specificity and high reproductive potential along with expanded immune gene repertoire property at the genetic level. This mosquito possesses the necessary potential to initiate and facilitate the disease transmission by establishing an effective vector-host transmission cycle for diverse pathogens in different environments. Thus, in the changing ecological conditions this mosquito might enhance its epidemiological importance in the near future as a smart vector for those pathogens which were isolated from this mosquito species but are presently not having any public health importance.

Keywords: *Culex quinquefasciatus*, Pathogen, Bio-ecology, Smart vector, Medical and veterinary importance

1. Introduction

The cosmopolitan distribution of *Culex quinquefasciatus* is across continents and ecozones mostly south of 39° N latitude [1]. This mosquito species has been subsequently introduced to New Zealand, Australia and other geographical regions by the anthropogenic activity. It is one of the most widespread mosquito species [2] found in the Eastern Asian region [3], Indomalayan, Australasia [4], Neotropics, Afrotropics [5] and pan and subtropical America [6]. The transmission of arbovirus is facilitated by biological vectors [7]. The principal source of arbovirus transmission is mosquito vectors [8]. The Southern House Mosquito, *Culex quinquefasciatus* is the principal vector of bancroftian filariasis and a potential vector of *Dirofilaria immitis* [9, 10]. This species is considered as a potential vector of West Nile virus (WNV) [11]. Additionally, it can transmit Alfuy, Almpiwar, Corriparta, Sindbis, Ross River virus, Japanese Encephalitis virus (JEV) [12], St. Louis Encephalitis virus (SLEV) [13], Reticuloendotheliosis virus [14], Murray Valley encephalitis [6], Edge Hill, Eubenangee, Getah, Kokobera, Koongol, Kowanyama, Kunjin, Mapputta, Stratford, Trubanaman, Wongal, Reovirus type 3 and Chikungunya virus [4, 14] in laboratory condition. Thus, evidently this cosmopolitan mosquito is a potential vector of many important pathogens causing concern to public health authorities (Table.1). This article is an attempt to review the bio-ecology, medical and veterinary importance of Southern House Mosquito, *Culex quinquefasciatus.*

2. Taxonomic Status of *Culex quinquefasciatus*

Culex quinquefasciatus is a member of globally distributed *Culex pipiens* species complex. Additionally, the *Culex pipiens* species complex has many related species, ecotypes and hybrids which are situated in geographical introgression zones on multiple continents [15]. *Culex quinquefasciatus* was first described in 1823 by Thomas Say from a specimen collected along the Mississippi River in the southern United States. At that time, a number of similar species around the world like *Culex fatigans* [16] from the Old World tropics were used synonymous to *Cx. quinquefasciatus* [17, 18]. Females of *Culex pipiens* and *Cx. quinquefasciatus* are morphologically indistinguishable and hybrid zones for the two species are well documented. Owing to this, *Culex quinquefasciatus* has been considered and designated as a subspecies of *Cx. pipiens* with the name *Culex pipiens quinquefasciatus* [19]. Studies have indicated that *Culex pipiens* and *Cx. quinquefasciatus* are two distinct sympatric mosquito populations [20] and they also exhibit a distinct and clear genetic difference [21] which led to the elevation of *Cx. quinquefasciatus* to a species status.

3. Origin and spread of *Culex quinquefasciatus*

Although previous studies stated that *Culex quinquefasciatus* was native to the low land regions of West Africa from where the species has been spread to tropical and warm temperate regions by human activity [22, 23], recent studies indicated that *Culex quinquefasciatus* originated in Southeast Asia and then established in the New World through slave ships and colonized Africa [24]. There are four major phases that are thought to have involved in the global expansion of this species. First of all, an introduction of *Culex quinquefasciatus* to the New world and Australia in lieu of its spread in the Old World tropics through sailing vessels included in the slave trade before 1800 [22]. Secondly, this species expanded to New Zealand, the islands of Hawaii, the Seychelles and archipelagos in the Pacific and Indian oceans through sailing vessels linked with the whaling industry of the United States of America during 19th century [25]. Thirdly, during World War II, the expansion of this species occurred to small Pacific atolls of military significance by army aircraft and ships [26]. Finally, this species expanded to the remote Pacific islands and Indian oceans through commercial airline travel [27].

4. Bio-ecology of Southern House Mosquito, *Culex quinquefasciatus*

4.1. Reproductive Biology and Breeding Behaviour

Gravid *Cx. quinquefasciatus* females lay a single egg raft averaging 155 eggs during each gonotrophic cycle; the number of eggs depends on mosquito age, blood source and blood volume [28]. Egg rafts are laid on the surface of a suitable water body selected, using the chemical cues derived from the conspecific egg rafts [29]. Larval to adult development is dependent on temperature, nutrition and population density and can be as short as at 7 days under optimal conditions (30 °C) [30]. Females mate within 2-6 days of emergence and may begin to seek hosts within 48 hours of emergence [28]. The duration of larval stages was 118 hours for males and 135 hours for females [31]. Females of *Cx. quinquefasciatus* emerge in large number than males in the regions where the seasons are more distinct [32]. Since this mosquito must require blood meal for reproduction and does not undergo a reproductive diapause, hence this species is active and reproduces year-round. In India, it may complete 2-3 gonotrophic cycles in a lifetime during the hotter season and 4-8 cycles in the cooler season [33]. It has been observed that infection with *Wuchereria bancrofti* could disrupt the relationship between mosquito size and egg production during the first gonotrophic cycle of *Culex quinquefasciatus* [33]. This mosquito was found in domestic collections of water and in places like flooded open cement drains, flooded latrines, overflow water from houses, kitchens, as well as in ground–pools, ditches and shallow wells. This species usually selects organically rich and polluted surface waters and artificial containers for breeding [6]. The species also breeds in shallow ponds, streams, phytotelmata [34] and also in artificial habitat such as drains, wells, septic tanks and other small containers [35]. While conducting a survey in metro rail construction sites in Kolkata, researchers found that *Culex quinquefasciatus* mainly preferred polluted water for breeding in winter and post-winter months [36]. In North Central Nigeria, Africa the Bancroftian filariasis is transmitted by *Culex quinquefasciatus* in urban and semi-rural areas where increased pollution of freshwater bodies and the introduction of pit latrines favour the breeding of the mosquito [37, 38]. A wide variety of sites, mostly characterized by coloured, foul water with high nutrient values and low dissolved oxygen content, such as pumping and irrigation wells, canals, wastewater treatment ponds, sewage overflows, rain pools, rice paddy fields, fish ponds, septic tanks, drains, cesspools, agricultural trenches, vegetable farms etc. generally are preferred as the breeding sites by this mosquito [39, 40].

4.2. Biting Behavior

Culex quinquefasciatus has a predilection for urban environments and feeds on human indoors as well as outdoors [41]. This mosquito is nocturnal and was found to be predominant of the total mosquitoes caught off human baits in Calcutta and adjoining South and North 24 Parganas districts [42, 43]. It constitutes 97% of the nocturnal man-biting mosquitoes of Calcutta [44]. In addition to human, the female can efficiently bite amphibians [4], pigs, horses, cattle, sheep, dogs, rabbits [14]. The annual transmission potential of brancroftian filariasis higher in the urban area than that in the rural areas [45]. *Culex quinquefasciatus* is considered as an opportunistic feeder in rural Bengal and feeds on blood of human (26.45%), ruminant (46.25%), pig (14.19%) and bird (6.45%) [46]. In Southern India this is a highly anthropophilic species, with 50-76% feeding on human [47]. Interestingly, it has been found that the attraction ratio of *Cx. quinquefasciatus* of man: cow was 101.1:1 in Burdwan district, West Bengal [48].

4.3. Seasonal Effects on population density

In tropical areas, population of *Culex quinquefasciatus* reaches the peak density during or just following the rainy season [28]. Interestingly, the peak population was found in the warmest months of the year in subtropical and warm temperate areas [49, 50]. In summer, the higher man hour density of this vector mosquito has been reported in Bankura, West Bengal [51].Adult female *Cx. quinquefasciatus* could survive till one month with a source of carbohydrates and at a constant temperature of 28 °C [52]. It has been documented that at lower temperatures (15 °C), longevity is increased dramatically [53].

4.4. Physico-chemical factors

The embryonic development of *Cx. quinquefasciatus* requires the optimal temperature ranging from 24 to 29 °C. It has been found that at Low (≤12 °C) and high (≥32 °C) temperatures the survivorship drops with an upper lethal threshold at 35°C. Slight alkaline water (<pH 8) with little (≤0.5%) NaCl, $CaCl_2$ and $NaCO_3$ are the favourable condition for the larvae [49].

4.5. Associations with other species

Many other mosquito species might co-exist with *Cx. quinquefasciatus* in peridomestic habitat, such as *Culex nigripalpus* in the southern United States [54] and *Culex australicus*, *Culex annulirostris*, *Culex pervigilans*, *Aedes polynesiensis*, *Aedes notoscriptus, Aedes hebrideus*, *Aedes* *pernotatus* and *Tripteroides melanesiensis* in the tropical Pacific [35, 55]. The larvae of *Culex quinquefasciatus* are occasionally found with *Aedes aegypti* and *Aedes albopictus* in domestic and peridomestic water containers [28]. *Cx. quinquefasciatus* larvae are often found in association with psychodid moth fly larvae in septic habitats [54, 56].

5. Genetics and Molecular Biology

Cx. quinquefasciatus has been extensively used for considerable genetic research because of its long-standing taxonomic controversy and importance as a vector [57]. The species contains three metacentric chromosomes among which Chromosome 1 is considered the shortest, Chromosome 2 is intermediate in length and Chromosome 3 is the longest [58]. The complete genome sequencing studies of *Culex quinquefasciatus* reveal that the number of their protein coding genes (18,883) is 22% greater than that of *Aedes aegypti* and 52% greater than that of *Anopheles gambiae*. In addition to this, the species exhibit multiple gene-family expansion which include olfactory and gustatory receptors, salivary gland genes and genes associated with xenobiotic detoxification [59]. It has been reported that the large cytochrome P450 repertoire of this mosquito species has a significant role associated with the mosquito resistance [60, 61]. Interestingly, research showed that *Culex quinquefasciatus* has the largest number of olfactory receptor among dipteran species which explains culicine olfactory behavioural diversity which is in turn related with their host and oviposition site choice [59]. The ability of this mosquito species to feed on birds, humans and livestock indicates that it has a large number of proteins which could increase their capacity to imbibe blood from diverse hosts [59]. In this context, it could be mentioned that researchers have also discovered a 16.7 kDa family of proteins following salivary transcriptome analysis [62].

6. *Culex quinquefasciatus* as an Invasive species

Culex quinquefasciatus has reputation as an important invasive species which exhibits significant detrimental impacts on resident species or ecosystem as well as human or vertebrate animal health [63]. Interestingly, being an urban mosquito, *Culex quinquefasciatus* has significantly also invaded lowland rainforest [64]. Moreover, the desiccation resistant egg is a significant characteristic of invasiveness of a species [63]. The serosal cuticle contributes to mosquito egg desiccation resistance [65]. The serosa has been considered as a protective layer around the insect egg. It secretes a chitinized cuticle, the serosal cuticle underneath the maternal eggshell [66, 67]. In mosquitoes, desiccation resistance coincides with the time of serosal cuticle secretion [68]. Studies indicated that *Culex quinquefasciatus* acquire desiccation resistance ability during embryogenesis through the formation of the serosal cuticle [69].

7. Insecticide Resistance

Culex quinquefasciatus control was mainly conducted through the use of neurotoxic insecticides belonging to the Organochlorines (OC), the Organophosphates (OP) and the Pyrethroids (PYR) families in the western Indian Ocean islands [70, 71, 72]. The larvae of *Culex quinquefasciatus* used to grow easily in sewers and waste water collections [73] where in addition to insecticides, they are also subject to a wide range of xenobiotics. The mosquito control failures in the field have been resulted from resistant *Culex quinquefasciatus* individuals [74]. The enzymatic detoxification (i.e. metabolic resistance) and target site modification are the two major insecticide resistance mechanisms found in mosquitoes [74]. The most common target modification in Culex quinquefasciatus are the L1014F mutation (kdrR allele) in the voltage-gated sodium channel gene, conferring resistance to PYR and DDT. The G119S ace-1 mutation (ace-1R allele) conferring resistance to OP and carbamates, while A302S Rdl mutation (RdlR allele) conferring resistance to the OC dieldrin [71, 75, 76].

8. Discussion

The importance of Southern House Mosquito, *Culex quinquefasciatus* as a mosquito vector from the public health standpoint relies on the fact that *Culex quinquefasciatus* is the principal vector of bancroftian filariasis and a potential vector of *Dirofilaria immitis* [9, 10, 77, 78]. It is also a competent vector of several arboviruses like West Nile virus (WNV) in northeastern United States [79] and Asia [80] St. Louis encephalitis virus (SLEV) in eastern and south-central North America [13], Rift Valley fever virus [81], and several protozoa like *Plasmodium relictum* that causes bird malaria [82]. Studies revealed that this mosquito species can efficiently transmit protozoan *Hepatozoon breinli* in the laboratory setup. *Culex quinquefasciatus* is also an important vector of avian pox [83, 84, 85] and *Plasmodium cathemerium* [4], a protozoan parasite of birds. Additionally, this species has also the ability to transmit the other nematodes like *Saurofilaria sp.*, *Oswaldofilaria sp.* [86]. The Southern House Mosquito is considered as a cyclopropagative vector for avian malaria and a mechanical vector for avian pox in Hawaii [87]. This vector is a well known domestic mosquito species of rural, semi-urban and urban areas [86, 88] and also has the reputation as an important invasive species [63]. The cosmopolitan distribution of *Culex quinquefasciatus* is across continents and ecozones mostly south of 39 °N latitude. This suggests that this invasive mosquito species has the plasticity to adapt in diverse habitats and this could be expanded owing to its amplified immunity gene repertoire [1]. Interspecific competition with the resident species in newly introduced areas may be the possible ecological process that might help this mosquito to become as a significant invasive mosquito species. In newly invaded areas, this mosquito species might also expand because of the absence of the suitable competitors and predators [63] (Table 2). Interestingly, researchers have found substantial mosquito samples from container-type breeding sites (metal and plastic containers, "calabash", and tyres) and least from phytotelmata [64]. The vast distribution of breeding sites (tires, plastic and metal containers, calabashes, puddles, leaf axiles, depressions on trees, etc.) possibly indicates the significant changes in the oviposition behaviour of *Culex quinquefasciatus* [64]. Studies indicated that the habitat quality in which mosquitoes are oviposited is the major factor behind enhanced offspring survival and growth. Thus, when the potential habitats differ in their suitability for juveniles, females used to select the habitats which can maximize the fitness of the juveniles [89]. The oviposition habitat selection in mosquitoes have been demonstrated in response to physical and chemical suitability for the larval development [90], which in turn might be the possible reason behind the variation in preference among metallic, plastic containers and calabashes as the suitable oviposition habitat [63]. Moreover, *Culex quinquefasciatus* mosquito can be able to survive in polluted waters where there are no natural predators, which leads to the excessive growth of their population [91]. *Culex quinquefasciatus*, thus indicates its adaptive flexibility [92, 93] and ecological plasticity. The changing climate might be associated with the substantial increase in the vector distribution, enhanced transmission potential especially in temperate climates, elongation of transmission season and shortening of vector gonotrophic cycle and incubation time [94]. *Culex quinquefasciatus* is a nocturnal mosquito [4]. Interestingly, the biting density, natural infection and infectivity rates of *Culex quinquefasciatus* were found significantly higher in the third quadrant of the night. This was true both in urban and rural environments [95]. Researchers demonstrated that the human foot region attracts *Culex quinquefasciatus* more than other parts of the exposed lower limb of the human host [96] (Figure. 1). This mosquito is thought to be capable of transmitting WNV [97].

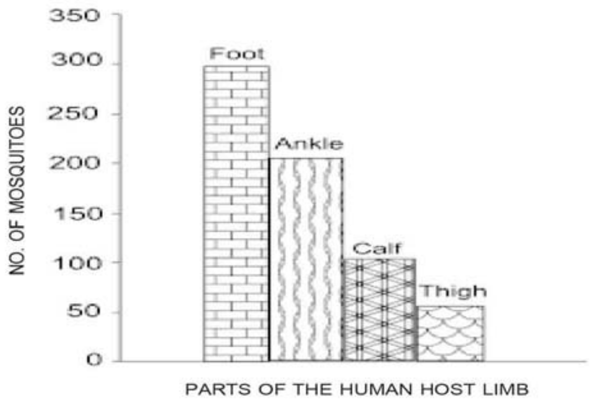

Fig 1. ***Culex quinquefasciatus*** **attracted to different parts of the human limb** [96]**.**

Although some members of *Culex pipiens* complex bite only birds and other members bite mainly mammals including humans [98], investigators reiterated that the Nearctic population of *Culex pipiens* complex feed on both bird and mammals. This selective feeding behaviour might be a possible reason behind the high frequencies of infection found in human, horse and bird by WNV in North America [99]. Albeit members of the *Culex vishnui* complex are important vectors of Japanese encephalitis [100], JE virus has also been isolated from *Culex quinquefasciatus* in several occasions [101, 102, 103]. Bhattacharya *et al*., [100] demonstrated that *Culex vishnui* supported JE virus for a longer period than *Culex quinquefasciatus*, however the Southern House Mosquito was able to generate a notable titre level for a considerable period of time (Figure.2).

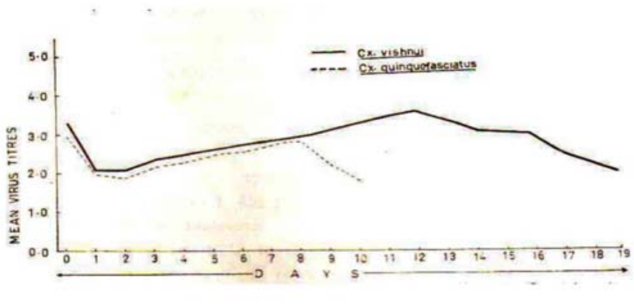

Fig 2. Duration of virus detection in ***Culex vishnui*** **and** ***Culex quinquefasciatus*** **mosquitoes**[100]**.**

JE is predomninantly a rural disease. Interestingly, JEV vectors are found in urban areas however, small in numbers [104]. Diverse pathogenic parasites, arbovirus and nematodes have been isolated from this mosquito species. Although the finding of any pathogen in particular species of mosquito is however not itself a proof that the species is a vector to the man or animal. The attainment of the status of being called a potential vector, itself is a dynamic phenomenon and there is a possibility that with the passage of time, *Culex quinquefasciatus* may become epidemiologically significant for some isolated pathogens (Table. 1) which are presently not having any public health importance.The arbovirus like JEV, WNV, SLEV survive by virtue of alternation between vertebrate and invertebrate hosts in a “cycle” where man gets the infection tangentially on accidental intrusion in this pathway. Animal hosts such as pigs and birds are recognized animal reservoirs and play an important role in the maintenance and amplification of these viruses. The mosquito vectors may carry the virus for life after getting the infection [105]. The Southern House Mosquito acts as an important “urban bridge vector” [106] which bridges different reservoir/amplifier hosts to humans because of its encounter with different vertebrates. This species also creates an ecological bridge between urban, periurban and rural areas owing to its presence in diverse ecological niches. Mosquito borne zoonotic viral disease like JE, is historically a rural disease which may spill over to urban areas in the changing ecological conditions; in such a situation *Culex quinquefasciatus* could play an important role not only as a bridge vector between man and pigs/birds (reservoir host) but also bridging the rural-urban eco-epidemiological zones. Hence *Culex quinquefasciatus* may emerge as a potential vector of urban Japanese encephalitis. Thus, ubiquitous *Culex quinquefasciatus* can act as both way traffic for the dissemination of certain zoonotic arboviral diseases in different environments. *Culex quinquefasciatus* is one of the most frequently encountered domestic and peridomestic mosquito among the other *Culex sp.* and mostly found in aboard aircraft [107]. The anthropophilic and endophilic blood feeding habits bring this species close to human and human habitation [103]. Thus, the remarkable adaptive fitness, ecological plasticity, invasive behaviour, host specificity, and high reproductive potential [103] along with expanded immune gene repertoire property at the genetic level [1] have made *Culex quinquefasciatus* a smart vector. This species possesses the necessary potential to initiate and facilitate the disease transmission by establishing an effective vector-host transmission cycle for diverse pathogens in different environments. Thus, it could be relevant to mention that in the changing ecological conditions Southern House Mosquito might enhance its epidemiological importance in the near future as a smart vector for those pathogens which were isolated/detected from this mosquito species. There can be a possible association between the invasiveness of this mosquito and the increased risk of introduction of pathogens in newer areas [108]. In this context, it could be mentioned that the insecticide resistance of *Culex quinquefasciatus* is a matter of concern as it might increase the risk of resurgence of parasitic and arboviral outbreaks. Global warming and globalization are likely to reshape the ecology of vector mosquitoes, such as ubiquitous *Culex quinquefasciatus* which might have a wide ranging consequences on the epidemiology of the vector borne diseases. This notion is also important in the context of emergence and invasion of arbovirus like Zika virus. Thus, a continuous surveillance and molecular studies are required to ascertain the prospective role of Southern House Mosquito, *Culex quinquefasciatus* in the possible transmission of different pathogens.

Table 1: List of virus and Protozoan and Nematode Parasite found and isolated from *Culex quinquefasciatus* in natural and artificial conditions

Pathogens detected/isolated in *Culex quinquefasciatus*	References
Virus	
West Nile virus (Flaviviridae)	11
Japanese encephalitis virus (Flaviviridae)	12, 100, 101
St. Louis encephalitis virus (SLEV) (Flaviviridae)	13
Rift Valley fever virus (Bunyaviridae)	81
Edge Hill virus (Flaviviridae)	4, 14
Eubenangee virus (EUBV) (Reoviridae)	
Getah virus (Togaviridae)	
Kokobera virus (KOKV) (Flaviviridae)	
Koongol virus (Bunyaviridae)	
Kowanyama virus (Bunyaviridae)	
Kunjin virus (Flaviviridae)	
Mapputta virus (Bunyaviridae)	
Stratford virus (STRV) (Flaviviridae)	
Trubanaman virus (TRUV) (Bunyaviridae)	
Wongal virus (WONV) (Bunyaviridae)	
Chikungunya virus (Togaviridae)	
Protozoa	
Hepatozoon breinli	26, 86
Plasmodium cathemerium	4
Plasmodium relictum	82
Nematode	
Wuchereria bancrofti	3
Dirofilaria immitis	10
Saurofilaria sp	86
Oswaldofilaria sp.	
Brugia malayi	36

Table 2: Features of invasiveness of *Culex quinquefasciatus* mosquito.

Location	Time of Introduction	Possible Ecological Processes	References
New Zealand	19th Century	Absence of Competitors and predators	109
Australia	19th Century	Interspecific competition via a gut symbiotic fungi	110, 111, 112
North merica	19th Century	interspecific competition with native *Culex* may have contributed declines of *Cx. tarsalis* in California	113

9. Conflict of Interest
There is no conflict of interest.

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