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Consanguinity as a Determinant of Profound Bilateral Sensory Neural Hearing Loss Disease among Deaf Children in Specified Rehabilitation Schools at Karachi, Pakistan

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Abstract

Introduction: Estimates of the magnitude of consanguinity related profound bilateral sensory neural non syndromic hearing loss (PSNHL) children in Pakistan are limited.

Methods: A descriptive study was conducted among deaf children age 0-18 year in three rehabilitation schools in Karachi in January 2020 that fulfilled the following case criteria: (1) Deaf child with profound sensory neural hearing loss (SNHL), pure tone audiometry (PTA), Brainstem Evoked Response Audiometry (BERA) and registered in a deaf school (2) presence or absence of self-reported kinship between the husband and his wife, (3) presence or absence of self-reported husband-and-wife part of a WATA SATA arrangement.

Results: A total of 714 children aged ≤18 years identified for confirmed PSNHL. Audiology findings from 260 (36.4 %) children met the criteria for confirmed PSNHL and consanguinity was detected in 235 of them (90.3%). The minimum detected prevalence of consanguinity related PSNHL in Karachi area was 7.1 per 1000 in children < 18 years of age. The average student age was 9.81 years with male (62%) predominance. The study population included males (62%) and females (38%) and ratio was 1.7:1. Most of PSNHL student (85%) belonged to 05–14-year age group. The majority of the respondents (69.6%) reported to have one deaf child in family. Nearly half students (43%) were of secondary class education formed the majority.

Conclusion: Mandatory pre-pregnancy & genetic counselling, non-consanguineous marital relation awareness, tele health, pro-bono medical and surgical services and consanguinity related PSNHL new born birth record registration is justified for inclusion in expanded programme of immunization card for early referral to best treatment modalities like cochlear implant surgery in Pakistan.

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Introduction

Consanguinity is an etiological factor of PSNHL disability among children that occur at prenatal stage worldwide. PSNHL in children arise from pre-natal damage due to parental consanguinity all over the world. It is well known that one third of disability is caused by genetic factors. Profound bilateral sensory neural hearing complete loss disability is present when audiology test pure tone threshold average is greater than 100 dB plus no open set speech recognition ability and hearing aids provide no benefits. At this level intervention must be considered [1, 2].

In profound sensory neural hearing loss, the non-syndromic hearing loss form accounts for approximately 70% of genetic deafness worldwide. Deafness when it occurs as an isolated symptom, it is called non-syndromic hearing loss. Non-syndromic hearing loss inheritance trends are autosomal recessive pattern (75%-80%) frequent in consanguinity, next pattern is autosomal dominant (20-25%) are frequent in post-lingual, non-consanguineous, progressive and lastly X linked or mitochondrial (1-2%). Non-syndromic hearing loss with autosomal recessive patterns behave exclusively monogenic, highly heterogenous, non-progressive, pre-lingual severe form of cochlear defects of hair cells and inherited deafness disease largely attributed to high rates of consanguineous marriages.

In consanguinity, the frequent form of autosomal recessive pattern is increased while autosomal dominant and mitochondrial pattern is decreased [3, 4, and 5]. Consanguinity is a more socio-economic and strong cultural preference isolated phenomenon specified in Pakistan. Burden of PSNHL disability varies in different population. Although paucity of past studies has estimated rate of PSNHL is 1.6-2 per 1000 in Pakistan. Consanguinity has also been shown to be responsible for one third of PSNHL disability cases born in consanguineous families [6,7]. Its burden is 1-2 in 1000 live birth in those countries where over a decade genetic counselling, surveillance, genetic screening and cochlear implant surgery activities has been part of routine health care services. The genetic diagnostic yield for consanguinity is less than 50% in hereditary hearing loss patients from European, African, North and South American and few Asian countries. Although, PSNHL burden increases to 3-4 per 1000 live birth with higher rates of consanguinity reflected in genetic diagnostic yield above 50% in Pakistan, Turkey, Iran and Saudi Arabia [8,9,10].

Consanguinity risk perception is variable mainly socio-cultural non-medical factors issues as hereditary complete hearing loss case management cochlear implant surgery is a less sensitive issue than non-consanguinity package low-cost intervention promotion in communities [11]. Newborn normal hearing is important for language and cognitive development, untreated complete hearing loss leads to impaired cognitive functions and learning competencies. Although, newborn hearing testing for example Oto-Acoustic Emissions (OAE), auditory brainstem response test is mandatory in many countries including Germany during the first three days to one month of life (Vona, B., Doll, J., Hofrichter, M. A., & Haaf, T. (2020)). Despite the availability, affordability and accessible equity cochlear implant surgery package, many hurdles have limiting many Asian countries from registration new born hereditary hearing loss in their birth certificate and expanded programmes on immunization card for early cochlear implant [12,13]. Cardinal obstacles are inadequate registry capacities, lack of national registry, lack of funding, surgery affordability, lack of trained personnel, lack of technology, low referral for cochlear implantation that has not been easy to demonstrate the estimates of disease magnitude and its expenditure to society.

There is a preventable factor has been the high expenditure of cochlear implant surgery compare to kidney transplantation in tertiary care setting [14,15,16]. A paramount among these is the need of update diseases frequency estimation critical in the decision to adopt cochlear implant surgery at tertiary care level. However, high and middle income countries in south Asia for example Kingdom of Saudi Arabia, Turkey, Iran have adopted state owned health financing in cochlear implantation expenditure for their citizens as Pakistan fall in lower middle income countries where cost matter in adopting effective cochlear implant surgery [17,18,19]. Few local and international otolaryngologists implant surgeon, private sector tertiary care hospitals and charity organizations are active and interested in pro bono services to fulfill this gap in Pakistan [20,21,22]. Approximately above one million children are deaf in Pakistan although less than 5% of theses have access to education in Pakistan [23]. There has been much debate on the seemingly quality of reporting burden of consanguinity related hearing loss in Asian countries specifically assumed estimate in Pakistan 6-8 birth per one thousand suffer from deafness [24]. However, consanguinity registration and its outcome is complex to estimate in poor resource settings. When enough resource availability has been made, consanguinity have been prominent etiology of newborn PSNHL

in few Asian countries including Pakistan [25]. Another little published information on the burden of "watta satta" (literally, a wedlock based on restriction of outflow of wealth within a family) economic marriage relationship and its isolations PSNHL is in urban population of Pakistan [26,27,28]. Furthermore, the rapidly growing population and paucity of studies in Pakistan, urge to assess the burden of PSNHL disability, consanguinity as timely screening for PSNHL at birth, counselling, awareness and cochlear implant services are important for the cases in Pakistan.

Realizing the importance of adequate descriptive survey and its case identification is relatively straight-forward and can yield accurate estimates of consanguinity related PSNHL prevalence by using the specially designed case proforma. The primary objective of our study was to determine the magnitude of profound sensory bilateral hearing loss in deaf children aged 0-18 years having consanguineous parents in three major urban centers of Karachi, a southern coastal metropolitan city in the province of Sindh, Pakistan. Another objective was to estimate "watta satta" among parents having PSNHL deaf children in three urban rehabilitation centers, Karachi, Pakistan. This information will enable stake-holders to understand the recent estimate of consanguinity related PSNHL and allocate rational decision on health financing, awareness but also enable donor, charity organization to raise funds and equity financial investment on cochlear implant surgery in Pakistan.

Methods

Study setting, design and period: This descriptive cross-sectional survey was conducted in three urban sites in a large metropolitan city Karachi from January 2020 to April 2021 that fulfilled the following criteria: Deaf child with profound sensory neural hearing loss, PTA report; presence or absence of kinship between the husband and wife; presence or absence of husband-and-wife part of a "WATTA SATTA" arrangement. Syndromic profound hearing loss and comorbidity profound hearing loss cases were excluded in initial screening at schools. All the major deaf rehabilitation schools were invited to participate in study but three non-governmental organization deaf rehabilitation school accepted the invitation and informed about the study. The consanguinity protocol was approved by the institutional review board of Jinnah Sindh Medical University (JSMU approval/IRB/2019/-262 dated 17th Feb, 2020).

Sample size and sample technique: The sample size was estimated by using proportion of consanguinity deafness as 1% at a confidence level 95% and bound of error 3%, the estimated sample size came out to be 1000. A consecutive sampling was used to collect the expected sample as it involved taking every PSNHL child who falls in the inclusion criteria over a specified time interval. During the study period any deaf child 0-18 year was eligible for the study if deaf child had registered for PSNHL at any of the schools in survey site and was resident of Karachi. Sample size was determined based on the proportion of newborn deafness reported by a subject expert observation.

Instrument, ethical considerations and data collection procedure: Principal investigator visited each major deaf school in Karachi and informed regarding the study. Participating schools were given briefing and training regarding study. Deaf school's permission was obtained before to carry out the study. Case report forms and consent form were given to school principal to further distribute among eligible study participants. Written consent, after explanation about the study, was obtained from the study participants. Participating deaf school returned the parent self-reported case report forms along with their hard copies of audiological assessment reports like PTA and BERA. The proforma was developed in English language and translated to Urdu language. Parent self-reported case report form and consent form were translated into urdu language. Informed consent was obtained voluntarily from the children and their parents/caretakers in study. Consanguinity information identified by self-parent administered record form. Complete hearing loss diagnosed by audiometric testing was available in school admission record and monitoring hearing loss treatment options, such as hearings aids, cochlear implants, surgery, oral-aural-manual rehabilitation, assistive devise, speech reading, sign language education training. Survey data were entered into a computer. Parents and their deaf child's name were not asked in case report form. Study participants had rights to withdraw from the study at any time. Confidentiality was maintained during research process acquired information treated private and securely stored and research and review ethics committee of JSMU approved the protocol.

Data Analysis: Data were entered and analyzed in SPSS, version 22 and Microsoft Excel. Descriptive statistics were performed for mean scores, frequency inference and percentages.

Results

Over the 15-month survey period (20 January 2020 to 30 April 2021), the survey have had detected 714 PSNHL children age 0-18 year among self-reported consanguineous families who had proven bilateral PSNHL. The total enrollment of deaf children in

three schools were 1378. Over 90% audiology result reports were from private sector audiology laboratories in the urban setting of Karachi, Pakistan. Table 1 gives the distribution of the study participants by demographic variables age, gender, deaf child in families and "watta satta" arrangement status in families. The mean ± SD of age of the participants was 9.81 ± 3.58 years. Nealy half of the students were 10-14 of age (43%) and two thirds (62%) were males. Majority of the respondent having single deaf child in a family. There were rare watta satta arrangement family (3.3%) among parents of PSNHL children in three schools at Karachi. Table 2 shows the distribution of consanguinity was 85% among bilateral profound sensory neural hearing loss children.

Variables		Frequency	Percentage (%)
Age (Years)			
0-4		35	4.8
5-9		306	42
10-14		307	43
15-18		66	10
Gender:			
Male		441	62
Female		273	38
Deaf child in families:	1	503	69.6
	2	115	15.9
	3	64	08.9
	4	20	02.8
	5	08	1.1
	6	04	0.6
Watta Satta in Families	Yes	23	3.3
	No	691	96.7

Table 1: *Frequency Distribution of Participants (n = 714).*

Age Group	Population in same age	No of Cases	PSNHL rate per 1000 population	95 % CL
0-18	714	619	7	83.6-86.3

Table 2: *Rate of Consanguinity PSNHL in Three Urban Deaf Schools.*

Discussion

Self-reported consanguinity was detected in 85% of PSNHL children age 0-18 years in Karachi making it the more common determinant of PSNHL in this densely populous metropolitan city of Pakistan. Consanguinity is very frequently seen among Pakistani citizen [29, 30, 31, 32, and 33]. Karachi is called a mini-Pakistan an economic urban hub located in south of Pakistan. Its population comprises of many ethnicities mainly Sindhi, Urdu, Punjabi, Pushto, Balochi, Gilgati, Kashmiri and Siraki. According to statistics, it has an incidence of 50-59% among Pakistani and Turkish citizens and 60-69% in Iran and Kingdom of Saudi Arabia (Vona, B., Doll, J., Hofrichter, M. A., & Haaf, T. (2020)). It has recently seen to have increased because of south Asian consanguineous belt. There was gender predominance as 62% of our cases were males and 38% were females.

A fairly rare percentage of our cases (14.4%) had a absent consanguinity status suggest not a common determinant of PSNHL. In this study consanguinity was defined a close kinship between husband and wife. Self-reported "watta satta" was 3.3% of PSNHL children in Karachi found rare in urban Karachi Pakistan. "Watta satta" (literally, a wedlock based on restriction of outflow of wealth within a family) is a common traditional practice (64-94%) in most of the rural Pakistan. "Watta satta" is an arrangement annulled on the ground of a bride exchange between families and families are blood relatives or non-blood relatives in Pakistan (Bhutta, et al (2015)). The tool was relatively simple which comprised of six questions covering child hearing status, parent consanguinity, watta satta status, PSNHL child age, child gender and number of hearing loss children in a family.

It was mainly designed for capture the consanguinity and PSNHL cases in deaf school-based survey although the cytomegalovirus past infection parent's recall bias information, place, duration of disability was not included. During the observational study period any deaf child age 0-18 year was eligible for study if he/she had confirmed bilateral non-syndromic pre-lingual complete deafness based on hearing tests PTA report results submitted at the time of admission in three deaf schools and was resident of Karachi. PSNHL cases were identified on research criteria or respondent self- reporting proforma in a consecutive sampling method at large urban deaf children settings. Nearly all the respondents who participated in the study and making it a representative study of population. Therefore, a total of 714 PSNHL children have been selected based on study criteria.

The small size of PSNHL cases was captured due to COVID-19 lock down, travel restrictions, schools were closed and CoVID-19 pandemic hesitancy among schools and resource poor urban setting. It took us about 14 months to access sample 714 consecutive PSNHL urban cases although tip of ice berg as not unusual for this study, it

represents a compromise between the aims of representativeness for population and adequate power and feasibility. The available literature suggests above three fourth marriages links from the same blood ancestor and most of marital relationships are within same tribe or clan in Pakistan [34]. Watta satta approximately accounts for one third of all marriages in Pakistan [35, 36, and 37]. There is no national newborn hearing screening nor national deaf new born registry at hospital or population based house hold national surveillance does not exist in Pakistan. In Karachi, the detected rate of 07 per 1000 in children age 0-18 years is just a new emerging scenario of consanguinity. Since, majority of PSNHL cases never admitted and screened due to parent low literacy, high cost of implant surgery and poverty in Karachi, Pakistan. Non-syndromic post-lingual hearing loss cases were excluded during study.

Therefore, the estimated rate of PSNHL of 07 per 1000 live birth is likely to be a minimum and significant under estimate due to limited resources. The other limitations were the number of cases per million population, lacking advanced diagnostic tests i.e. genetic testing, past infection for example cytomegalovirus etc in PSNHL. An additional information regarding status of parent's "watta satta" marital relationship arrangement sought as a contributory factor influencing consanguinity may correlate with number of PSNHL children. Further local large sample studies are needed to examine whether the disproportionate burden of PSNHL in relation to consanguinity is being updated. Every nation requires that its citizen be healthy and productive. This mainly depend on healthy conception, preventive screening for genetic factors, genetic diseases including consanguinity is an important element in dealing possible PSNHL early, thus enabling timely cochlear implant intervention.

This effort reduces the expression and severity of PSNHL in children. Early cochlear implant surgery in PSNHL children influence well on personality development of child. If left untreated PSNHL child never develop speech & further disrupt their social and emotional development of particular distress is that these children and their families are under stress and require timely cochlear intervention in order to help the children, family have a normal life (Shearer, et all (2019).). Although prevention of manifestation of PSNHL disability include genetic counselling and genetic screening is important for the control of consanguinity determined PSNHL disability in family. Early identification of PSNHL condition after birth followed by prompt cochlear implantation successfully reduce the burden of PSNHL disability in Pakistan. PNSHL is the severe form of congenital permanent deafness disease in children among consanguineous couple.

The recommended age for cochlear implantation is as early as one year of age but not above four years of age preferably in the first five year of life of PSNHL child. Although early detection of hearing loss and timely cochlear implantation is important for maximal auditory performance as apparently etiology have no role. However, PSNHL children (> 90 db HL) at least 2 years or older are candidates for cochlear implantation in United States of America (Shearer, et all (2019)). In young children, auditory brainstem response, OAE testing, auditory behavioral responses and stapedial reflexes are useful to determine the hearing status. We have captured 7% of the cases of PSNHL in Karachi, Pakistan as could estimate prevalence of 6-8 new born babies per 1000 live births which is considerable and true status to rates observed in low-income countries. Therefore, the prevalence of PSNHL in children in Pakistan is estimated at 7-8 per 1000. We have concluded that consanguinity related PSNHL is the commonest factor that has influenced the children with deafness in Pakistan. There is a noticeable size of family clumping towards marital relationship within families of Pakistan. It is thus an alertness based on the magnitude of deafness and thalassemia to include consanguinity related PSNHL recorded in new born routine immunization card, offered genetic counselling and cochlear implantation awareness campaign in Pakistan. Therefore, preventive consanguinity awareness should implement in school health programme. Further research is needed to look the intervention and its impact on treatable proportion of deafness.

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Conflict of Interests

The authors declare that there is no conflict of interest.

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