Research Article

Prevalence of Congenital Defects among Consanguineous Marriages in Pakistan

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Abstract:

Background: Consanguineous marriages are marriages within the family i.e between two first cousins. It has been discovered that a greater risk of developing congenital defects in the progeny is observed if the parents are related. In Pakistan, due to cultural and religious trends, marriages within families are rising with time and this leaves Pakistan among the top few countries which have been a common interest of investigators, social scientists, medical researchers, biologists, and physicians who are interested in congenital abnormalities that are inherited from consanguineous parents. The goal of our study is to evaluate the prevalence of congenital defects in children who are a result of consanguineous marriages in the region of Pakistan and also highlight the possible hindrances in further investigation and prevention of congenital defects in children of related parents. This will help us in identifying the extent of this problem and possible policies that can be implemented to reduce congenital abnormalities in Pakistan.

Methodology: We looked for, gathered, and assessed literature that reported the prevalence of congenital defects in children of consanguineous marriages in the region of Pakistan from 2014 to 2022 on PubMed, Google Scholar, and Cochrane. Combination keywords such as consanguineous marriages, consanguinity, congenital defects, congenital disorders, congenital malformations, congenital diseases, congenital disabilities, and Pakistan have used Full-text original studies in the English language done from 2014 to 2022 were included. The search was carried out following PRISMA standards.

Results: We identified 10 articles that met the criteria set for selection based on our topic of research. The results showed that there was a significant increase in congenital abnormalities if the Parents of that child were consanguineous. Consanguinity influenced the number of stillbirths and abortions as well and in children born to such parents 2 to 4 percent of live births and congenital abnormalities of physical, mental, or cosmetic origin. It was analyzed that parents who were first cousins had greater incidences of having a congenitally inherited abnormality than second or third cousins. There were fewer chances of developing congenital disorders in children whose parents were unrelated.

Conclusion: It is concluded that parents who are related by blood have a higher incidence of having babies with mental retardation, congenital deafness, congenital heart disease, and various other autosomal recessive disorders. Therefore it's the need of the hour to create public awareness to lower the risk of congenital defects and improve the facilities of genetic testing in Pakistan for early detection and improvement in the living standard of affected children. Our study serves to create awareness among families to avoid consanguineous marriages and urge to improve the community programs for children born with a congenital defect.

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Keywords: Consanguineous marriages, consanguinity, congenital defects, congenital disorders, congenital malformations, congenital diseases, congenital disabilities, and Pakistan.

INTRODUCTION:

Consanguineous marriage is the marriage within the family between two first cousins. The Hallmark of consanguineous marriages is congenital defects among offspring. Pakistan has been showing the highest trend of consanguineous marriages. Consanguineous unions have remained under continuous investigation by social scientists, medical researchers, biologists, and physicians. However, it received less attention in mainstream demographic research. (6) Major congenital abnormalities or birth defects carry significant medical, surgical, cosmetic, and lifestyle consequences. Such abnormalities may be syndromic, involving multiple organ systems, or can be isolated. Overall, 2% to 4% of live births involve congenital abnormalities.[7] The risk for birth defects in the offspring of first-cousin parents is substantially higher than in the offspring of non-consanguineous parents. An investigation of the trend of consanguineous marriages in Pakistan from 1990 to 2018 presented its strong association with increased rates of abortion, stillbirths, pregnancy terminations, low birth weights, increased mortality, and congenital malformations. Findings revealed that consanguinity contributes significantly to women's reproductive health and fertility behaviors [1]. The detrimental recessive gene expression in consanguineous progeny has contributed to the overall disease profile in both developed and developing countries and has highlighted potential genetic problems [2]. [3] This study has established a significant role of parental consanguinity in congenital heart diseases but the effect of consanguinity on genetic diseases is not uniform and this should be taken into consideration in genetic counseling Moreover, Clinical and audiological studies of patients with progressive sensorineural hearing loss were carried out and showed a role of consanguinity [4]. A study also showed that sixty-six percent of patients with auditory neuropathy spectrum disorder were born of consanguineous marriages [5]. This study is substantial as the prevalence of consanguineous marriages may significantly lead to various health-related implications. Previously conducted research lacked in explaining different aspects of this problem. Since consanguineous marriage is one of the major causes of congenital defects and physical disabilities in newborns, this research wants to address this issue in society. The rationale is to spread awareness among the public masses about the aftermaths of this issue. Being more prevalent in the Muslim community, consanguineous marriages are considered quite normal, thereby promoting screening can help diagnose aberrations earlier.

METHODS AND METHOD:

Strategy:

The search approach adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (9) and the PRISMA guidelines were followed throughout. An extensive systematic search of three electronic databases; PubMed, Google Scholar, and the Cochrane Library was undertaken. Studies are done between 2014 and September 2022 were selected.

A combination of the following terms was used for

the search:

Category 1: Population (Children of consanguineous marriages couples of Pakistan).

Category 2:Disease (Congenital defects and congenital diseases).

Category3: Prevalence for Epidemiology.

With the search criteria mentioned above, a new search was run on each electro-search engine one by one. Additional publications were found by manually searching the reference list searches. The articles were added on the Mendeley desktop and duplications were removed. Initially, the articles were reviewed based on title and abstract followed by full article reviews.

Inclusion & Exclusion Criteria:

Exclusion Criteria:

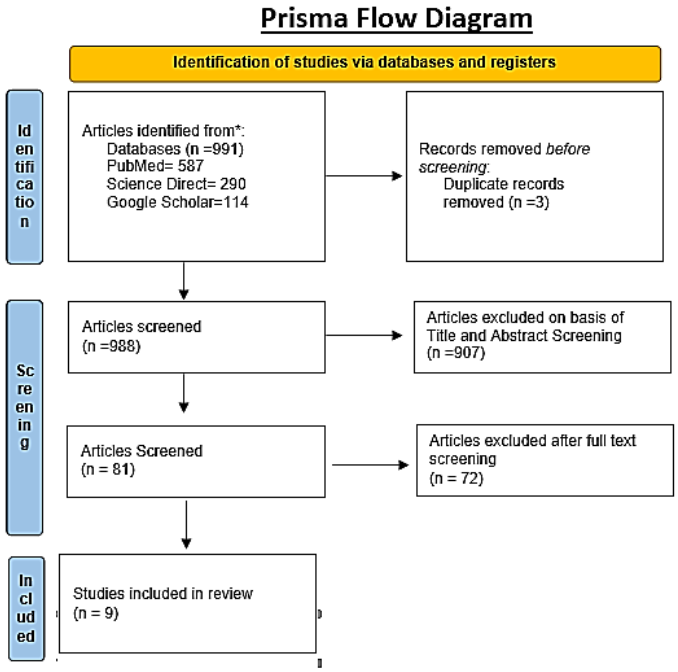
1. All the articles with language other than English were excluded.
2. All the articles with populations other than the Pakistani population were excluded.
3. All the articles whose full article wasn't available were excluded.

Inclusion Criteria:

1. Cross-sectional study.
2. Population –Pakistani.
3. Consanguineous marriages couples and their children.
4. Studies involving congenital defects among them.

OBJECTIVES:

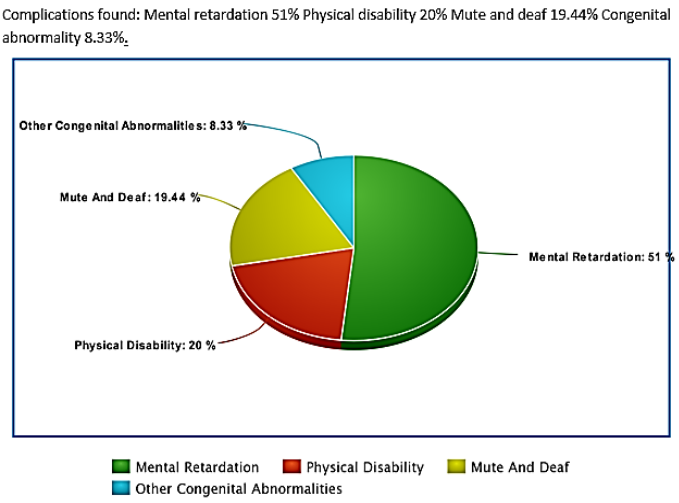
To determine the prevalence of congenital defects resulting from consanguineous marriages in Pakistan.



RESULTS:

9 studies were selected following PRISMA guidelines. The prevalence of congenital abnormalities among children of consanguineous marriages was very high. 35 percent of children as a result of consanguineous marriages suffered from a genetic disease or postnatal death.

Complications found: Mental retardation 51% Physical disability 20% Mute and deaf 19.44% congenital abnormality 8.33%.



Finding Table:

Title	Author	Journal	Database	Type Of Study	Year of Publication	Prevalence of Consanguinity	Population	Incidence of children with congenital defects	Correlation With parental education/ socioeconomic status	Limitations
Causes of deafness in the Punjab region of Pakistan and the role of consanguinity	S. Ullah, M.Aslamkhan, A.AliM.Idrees	Public health	Science Direct	Observational study	2017	80%	Population of Punjab	0.202% The percentage of deaf males and females was 0.220% and 0.181%, respectively	Not Found	Language-specific Limited population included
Knowledge, Attitude, and practice of consanguinity and its associated reproductive risks in a rural population of Charsadda, Pakistan	Aisha Liaqat, Hameed Ur Rehman, Asma Abdul Rehman, SafaAnwar, AnamKhurshi, H Hameed Allah, Mohammed Usman Afridi, Mohammed Ibrar	J Med Stud.Vol. 2, No.2,2016	Researchgate.net	Cross-sectional study	2016	57.67%	The rural community of Nah aki, Charsadda, KPK province of Pakistan	35 percent of children as a result of consanguineous marriages suffered from a genetic disease or postnatal death Complications found: Mental retardation 51% Physical disability 20% Mute and deaf 19.44% Congenital	Low socioeconomic status, age at marriage, family pressure, cultural norms, and traditions	Time-bound Questionnaire in English. Major language barrier The majority of the population was illiterate

								abnormality 8.33%		
Diagnostic and perinatal outcomes in consanguineous couples with a structural fetal anomaly	Mone F, Doyle S, Ahmad A, Abu Subieh H, Hamilton S, Allen S, Marton T, Williams D, Kilby M.	Actaobstetricia et gynecological Scandinavica.	Pubmed	The retrospective and partially prospective Cohort study	2020	Consanguineous pregnancies studied were 62	UK-based study. Most consanguineous couples were of Pakistani ethnicity (odds ratio [OR] 29, 95% confidence interval [95% CI] 13-62)	The risk of perinatal death was greater (OR 3, 95% CI 1-6) in the consanguineous group, as was the risk of fetal structural anomaly recurrence in a subsequent pregnancy (OR 4, 95% CI 1-13)	Not Found	1-The study's predominant retrospective nature. 2- Selection bias 3- The study took place over a decade. 4- Results cannot be concluded for Pakistanis or Bangladeshis or Muslims
PREVALENCE OF CONGENITAL DISEASES AMONG CONSANGUINEOUS MARRIAGES IN DISTRICT PESHAWAR PAKISTAN CM	Sarwar N, Nawaz R, Abid S, Hamza A, Khan A, Durrani A, Khan W.	aahs.kmu.edu.pk	aahs.kmu.edu.pk	Cross-sectional study	2020	73.5%	Outpatient departments of the different private and public hospitals of Peshawar	11(4.8%)children had Down Syndrome followed by congenital heart defects (n=13,5.7%), thalassemia (n=190, 82.6%), Mentalretardation (n=5, 1.7%) and Charcot Marie Tooth Syndrome (n=12, 5.2%)	The present study Was similar to the former study and demonstrated subjects who were belonging to poor families had an extremely high frequency of low socioeconomic status 110 (47.8 %)	Time-bound Questionnaire in English.Major language barrier The majority of the population was illiterate

Association of Consanguineous Marriages with Congenital Birth Defects	RabiahRiaz, Maria Inayat, Faiza Aslam	Journal of Rawalpindi Medical College Students Supplement	journalrmc.com	Case-Control study	2016	Not Discussed	Patients presenting to the department of gynecology and obstetrics of Holy Family Hospital Rawalpindi		Not Discussed	Only patients presenting to a certain hospital were taken into the study. Only a certain age group (18-35Y) was targeted.
Consanguinity and Neural Tube Defects	NuzhatNauman, ShireenRafiq, Saminajalali, SajjadAslamShami, Nadeem Akhtar	Journal of Rawalpindi Medical College (JRMC)	journalrmc.com	Case-Control study	2016		Patients presenting to the department of gynecology and obstetrics of Holy Family Hospital Rawalpindi.		The majority of the patients had low socioeconomic status.	Only diagnosed patients were taken into the study. A proforma was filled and there could have been a language barrier as the majority of the patients were illiterate.
Estimating the Inbreeding Depression on Cognitive Behavior: A Population-Based Study of Child Cohort	Mohd Fareed, Mohammad Afzal	PLOS One	Pubmed.gov	Cohort study	2014	42%	The Muslim population of the Jammu region	The ratio of consanguinity was 9% higher in people with low SES.	The only Muslim population was selected. Children of age 6-15 were selected only. No schooling children and children with congenital defects were also excluded.	IQ tests were performed by a person and data collected was recorded on a questionnaire.

Effects of consanguineous marriages on perinatal outcome	AbeeraChoudry, Maria Habib*, ZainabShamem*, SyedaZubdaBatool, ShafiaBarkat, MishalNaseem, Salma Nisar	Pak armed forces med journal		Cross-sectional study	2020	First-cousin marriages accounted for 31.1%, second-cousin marriages 14.3% and those not in relation were 54.6%.	Patients presented in Pak Emirates Military Hospital			
Analysis of the frequency of congenital fetal anomalies diagnosed on antenatal ultrasound in a tertiary care hospital in Balochistan	AmeetJesrani, Pari Gul, ShamaJogezai, Palwasha Gul, FahmidaNaheed, Asif Jamal.	International Journal of Reproduction, Contraception, Obstetrics, and Gynecology	Google Scholar	Cross-Sectional Study	2019	2.5%	Patients in the department of Radiology, Bolan Medical Complex Hospital Quetta	Nil	Mothers Aged 25-29 had a greater prevalence of cases as compared to other age groups in the study. Most cases were related to CNS abnormalities Mothers taking folic acid had less incidence of congenital defects as compared to others.	Only the cases in the given hospital were included Only ultrasound was used as means of diagnosis.

Quality Assessment:

Each paper was initially screened and analyzed separately by two authors (NA & SA) before being included or excluded. Articles were further evaluated by the other five authors (NA, SA, SH, SI, SM) to see whether they met the inclusion and exclusion criteria. The titles and abstracts of each publication were initially reviewed to see if the selection criteria were met. The complete text of any articles that didn't fit these requirements wasn't obtained and was excluded. When there was a difference of opinion about the eligibility, the four authors (SI, SA, SH, and NA) reasoned and decided whether or not to include or exclude that specific article. Additionally, the included studies were assessed for quality by The Joanna Briggs Institute (JBI) critical appraisal tools for prevalence studies. All studies that fulfilled the eligibility criteria were included in the review regardless of their quality assessment results. A detailed assessment of the included articles is shown in table 1. Following were the results for the mentioned 9 studies: 4 (44.44%) were of very good quality, 4 (44.44%) were of good quality, and 1 (11.11%) was of average quality.

Sr. No.	Author	Joanna Briggs Institute Score	Was the sample frame appropriate to address the target population?	Were study participants sampled appropriately?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there an appropriate statistical analysis?	Was the response rate adequate and if not was the low response rate managed appropriately?
1.	S. Ullah et al.	8	Yes	Yes	Yes	Yes	Yes	Yes	Yes	unclear	Yes
2.	NaveedaSarwar et al.	8	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
3.	AbeeraChoudry et al.	8	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
4.	FionnualaMone et al.	6	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes
5.	RiazRabiah et al.	9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6.	NoumanNuzhat et al.	9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7.	Liaqat Aisha et al.	8	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
8.	JesraniAmeet et al.	9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9.	Fareed Mohd et al.	9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

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DISCUSSION:

S. Ullah et al. conducted another study in the Punjab province of Pakistan about the causes of deafness and the role of consanguinity. This study showed that cousin marriages are more common in the district of Chakwal, as is the prevalence of congenital deafness. Another similar study was conducted in the Palestinian population on genomic analysis of inherited hearing loss. It showed that the number of families with recessive hearing loss due to homozygous mutations would decrease by 99% if the families were non-consanguineous.1 The genetic analysis revealed that consanguinity is responsible for the prevalence of deafness and the distribution of genes responsible for it in the Palestinian population.1 So there is a clear correlation between the prevalence of inherited deafness and consanguinity. These cases of deafness can be prevented by proper counseling of families and pre-marital genetic testing in cousin marriages.

Dr. Fionnuala Mone et al. conducted a retrospective and partly prospective cohort study comparing consanguineous (n=62) and non-consanguineous (n=218) pregnancies with fetal structural anomalies in a UK prenatal genetic clinic from 2008-2019. Most consanguineous couples were of Pakistani ethnicity OR 29 (95% CI, 13-62). In the consanguineous group, the uptake of prenatal invasive testing was lower compared to the non-consanguineous group. This likely explained the lower proportion of consanguineous couples where a final definitive unifying diagnosis to explain the fetal structural anomalies was reached. When a diagnosis was obtained in this group, it was always postnatal and most often using genomic sequencing technologies. The risk of perinatal death was greater OR 3 (95% CI, 1-6) in the consanguineous group, as was the risk of fetal structural anomaly recurrence in a subsequent pregnancy OR 4 (95% CI, 1-13).

Abeera Choudry et al. conducted a study at Pak Emirates Military Hospital Rawalpindi. Patients were divided into consanguineous and non-consanguineous groups. There were 1381 participants included in the study. First-cousin marriages accounted for 31.1%, second-cousin marriages 14.3% and those not in relation were 54.6%. Consanguinity had a significant association with age and ethnicity. Significant association with consanguinity was found for threatened preterm labor, preterm delivery, nursery admissions, and neonatal outcomes. Low education was found to be 2.46 times more likely to be with consanguinity. The study concluded that consanguinity is very common in Pakistan, especially in some ethnic groups (1.75 times more in Pathan ethnicity). Despite targeting a homogenous group, consanguineous marriages were associated with a much higher risk of NICU admission, stillbirth, and perinatal mortality.

Moh Fareed et al. conducted a study that is one of the first attempts with details of inbreeding coefficients and elaborate statistics to examine the effects of inbreeding on the cognitive abilities of children among the indigenous Muslim populations of the Jammu region (Northern India). Our results showed a significant decline in cognitive abilities of children

due to inbreeding and a higher frequency of mental retardation observed among offspring of inbred families, whereas children from non-consanguineous families display higher values of VIQ, PIQ and FSIQ scores and consequently the low frequency of mental retardation or ID. Various studies on consanguineous marriages and other forms of inbreeding have cited a discernible reduction in cognitive abilities, with increased mental illness in the offspring of such unions [26,51–53]. A familial study has reported the incidence of mental retardation among the children of first cousins being four times greater than that in the control group [54]. The study of Morton [51] has revealed that the offspring of first cousins had over five times higher risk of mental retardation when compared to that of the control. The study concluded that a decline in IQ or an increase in the frequency of mental retardation were consistent with rare recessive alleles associated with around 325 loci, whose likelihood of being transmitted to offspring increases with the relatedness of the parents.

Naveeda sarwar et al. conducted a cross-sectional study in the rural population of KP province showed that only 29.7% of the people knew about the risks associated with consanguineous marriages, and only 4.3% had undergone blood testing for genetic status before marriage. These results show the lack of awareness in the rural population about the risks. 97.3% of people reported cousin marriages in their extended families, and the main reasons were family pressure, low socioeconomic status, and lack of awareness about the reproductive dangers associated with it. The prevalence of consanguineous marriages is very high among the rural population. We need to create mass public awareness through media and reach out to rural areas to educate these people about the reproductive risks associated with cousin marriages.

Similar to studies in our systematic review, Mohd Younis et al. mentioned that the rate of consanguinity is high among the Muslim community around the world. Many rare genetic disorders and new genetic syndromes, congenital malformations, morbidity, mortality, and reproductive wastage have been observed to increase the frequency of consanguineous marriage. Some other abnormalities include low birth weight, cleft lips, congenital heart defects, and neurological defects.

Mohd Fareed et al. stated that more than 1.2 billion of the current global population practice consanguineous marriage. The most common form of consanguineous union is contracted between first cousins, in which the spouses share 1/8th of their genes inherited from a common ancestor and so their progeny is homozygous at 1/16th of all loci. Parental consanguinity has been associated with an increased risk of adverse prenatal outcomes and many other complex disorders.

CONCLUSION:

There is an increased risk of congenital defects among consanguineous marriages in Pakistan. Children of such couples have an enhanced risk of developing physical and mental abnormalities. They are at higher threat to suffer from mental retardation, congenital deafness, congenital heart diseases, Charcot-Marie Tooth Syndrome, and autosomal

recessive disorders. There is a dire need for mass awareness campaigns and counseling sessions among the public so that people could comprehend the greater risk of developing congenital defects and autosomal recessive disorders among the consanguineous couple's children. In this way, we can reduce these preventable disorders in our country.

Strengths and Limitations:

The systematic review finds its strength in the fact that a rigorous methodology was used to perform it and was accomplished according to a published protocol. The search strategy was carefully developed and comprehensive in nature. The search strategy was carefully developed and comprehensive in nature. The review was restricted to articles covering a period of 2014 to 2022 to give more relevance to the current situation and for purpose of planning realistic interventions. All the studies added to the review were cross-sectional and had different sample sizes. More highly powered studies are needed to find out the prevalence of congenital defects among consanguineous marriages in Pakistan would be needed to fully address this topic.

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