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# CONSANGUINEOUS MARRIAGES AND THALASSEMIA MAJOR IN PAKISTAN: A CROSS-SECTIONAL STUDY ON AWARENESS AND PREVALENCE

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**Abstract**
Background: This study aimed to investigate the association between cousin marriages and the risk of Thalassemia major in Pakistan, while also assessing the awareness levels of affected patients regarding the disease and their inclination towards premarital carrier screening, prenatal diagnosis, and preconception genetic counseling.
Introduction: Thalassemia major stands as one of the most prevalent inherited diseases in Pakistan, attributed to various genetic defects hindering globin chain synthesis. With approximately 5000 new cases diagnosed annually and over 50,000 registered Thalassemia patients receiving treatment across the nation, the disease poses a significant public health concern.
Study Design: A descriptive cross-sectional study was conducted at the Thalassemia blood center, Hilal-e-Ahmer trust hospital in Sargodha, from March 2022 to October 2022. A pretested predesigned close-ended questionnaire was utilized to collect data from a sample size of 200 participants, comprising Thalassemia patients resulting from cousin and non-cousin marriages. The study obtained approval from the ethical review committee of the institution before commencement.
Results: Our findings revealed a slight male predominance, with 54% males and 46% females. Cousin marriages accounted for 79% of patients, highlighting the significant influence of genetic factors in Thalassemia major prevalence. Among families, cousin marriage was prevalent in 86% of cases. Additionally, 52% of parents of Thalassemia patients became aware of their carrier status after undergoing screening.
Conclusion: The high prevalence of cousin marriages in our sociocultural context contributes to the persistent increase in Thalassemia major cases. Furthermore, inadequate awareness among affected individuals underscores the need for comprehensive education initiatives targeting the general public, parents, and families of Thalassemia patients.

**Keywords** Thalassemia major, consanguineous marriages, screening tests, blood transfusion, autosomal recessive.

## INTRODUCTION

Thalassemia encompasses a spectrum of autosomal recessive disorders characterized by diminished hemoglobin production due to faulty synthesis of alpha and beta chains, leading to increased destruction of red blood cells (1). Individuals with alpha thalassemia exhibit insufficient alpha chain production, resulting in an excess of beta globulin chains, while those with beta thalassemia lack beta globulin chain synthesis, leading to an excess of alpha chains (2). Globally, thalassemia ranks as the second most prevalent hemoglobinopathy following sickle cell disease (3). Thalassemia major has emerged as a significant public health concern, being identified as the most prevalent genetic blood disorder globally by the World Health Organization (WHO) (4). The burden is substantial, with approximately 70,000 infants born with beta Thalassemia major annually worldwide, and an estimated 270 million individuals carrying hemoglobinopathies (4). In addressing these challenges, literature provides a comprehensive overview of global thalassemia epidemiology and discusses recent advancements in prevention and management strategies. It also explores the impact of consanguineous marriages on genetic disorders, including thalassemia, shedding light on the implications for clinical genetics and public health (5,6).

The incidence of beta thalassemia major is notably higher in tropical and sub-tropical regions, particularly in Mediterranean countries, South East Asia, the Middle East, and the Indian Subcontinent, with reported higher carrier frequencies in specific regions such as Cyprus, Sardinia, and South East Asia (7). Notably, nearly 70% of families in the present study reported having more than one child with beta thalassemia major (8). In Pakistan, thalassemia major stands as one of the most prevalent genetic disorders, with over 5000 new patients added to the affected population annually (9). The prevalence is exacerbated by the deeply ingrained social practice of cousin marriage, which constitutes approximately 60% of marriages in Pakistan and contributes significantly to hereditary disorders (10).

Different studies shed light on the knowledge, attitudes, and experiences of individuals undergoing genetic counseling and prenatal diagnosis in Pakistan, highlighting cultural factors influencing decision-making regarding genetic testing and family planning (11, 12).

Cousin marriage, defined as marriage between individuals with an inbreeding coefficient equal to or greater than 0.0156, substantially elevates the risk of thalassemia major in offspring (13). Recent studies have underscored additional social and cultural factors, including low economic status, lack of awareness, and intra-ethnic marriages, as further contributors to the high frequency of thalassemia in the Pakistani population (14,15). This is corroborated by a study which discusses the challenges encountered in managing beta-thalassemia and emphasizes the need for comprehensive care strategies to improve patient outcomes (16).

Presently, two main treatments for thalassemia major exist: symptomatic management and bone marrow transplantation (1). However, there is no definitive cure, and lifelong blood transfusions constitute the primary form of treatment, imposing significant financial and emotional burdens on affected families and the healthcare system (1). The exploration of thalassemia's psychosocial effects on patients and their families underscores the significance of comprehensive care strategies that cater to both medical and psychosocial requirements (17).

The primary aim of our study was to investigate the correlation between cousin marriages and the prevalence of beta thalassemia major, while the secondary objective was to evaluate parental knowledge of the disease and attitudes toward prenatal diagnosis, particularly in Sargodha, where social and caste-based marriages are prevalent.

## METHODOLOGY

### Study Design

This study adopts a descriptive cross-sectional design.

### Setting

The research is conducted among patients diagnosed with thalassemia major, who are attending the thalassemia blood center at Halal-e-Ahmer Hospital in Sargodha.

### Duration

Data collection spans from March 2022 to October 2022.

### Sample Size

A total of 200 patients are included in the study. The sample size is determined with a p-value of 0.05, resulting in a margin of error of 6.9% (alpha=0.069) and a confidence level of 95%. The sample size calculation is based on the formula S= Z^2xPxQ/E^2, = (1.96)2x (0.5) x (0.5)/ (0.069)2 yielding a value of 200.

### Exclusion Criterion

Patients with other hemoglobinopathies, such as sickle cell disease and hereditary spherocytosis, are excluded from the study.

### Inclusion Criterion

The study includes patients diagnosed with thalassemia major, as well as their parents.

### Data Collection

Prior to the main data collection, a pilot study is conducted to assess the reliability of the questionnaire. The questionnaire covers various

aspects including demographic information, frequency of cousin marriages, awareness about preconception genetic counseling, screening methods, genetic modes of transmission, the preventable nature of thalassemia major, and opinions regarding future cousin marriages. Anonymity and confidentiality of the participants are strictly maintained throughout the data collection process.

## RESULTS

A survey was conducted to check the frequency of Thalassemia major among males and females in families who have had cousin marriages, their awareness about the disease in the parents of the patients and their point of view about Thalassemia screening and abortion of Thalassaemic child. Survey was conducted in thalassemia blood centre, Halal-e-Ahmer hospital, Sargodha.

### Social and Demographic Characteristics

The demographic characteristics of the study participants showed a slight male predominance, with 54% males and 46% females.

The age distribution of the participants ranged from 2 to 21 years, with a mean age of 8.33. The majority of the patients fell within the age group of 6-10 years, comprising 36% of the study population. This age distribution highlights the vulnerability of children in this age range to be affected by Thalassemia major.

**Table 1**: Table illustrates the age distribution of study participants, presenting the frequency and percentage distribution across various age intervals ranging from 1 to 25 years. The table highlights the proportion of participants within each age group, providing insights into the age demographics of individuals affected by Thalassemia major in the study population.

| Age interval | Frequency | Percentage % |
|---|---|---|
| 1-5 | 66 | 33 |
| 6-10 | 72 | 36 |
| 11-15 | 48 | 24 |
| 16-20 | 10 | 5 |
| 21-25 | 4 | 2 |

### Frequency of Thalassemia Major and Marital Patterns

Furthermore, the survey demonstrated that 79% of the patients were the result of cousin marriages, emphasizing the influence of genetic factors in the prevalence of Thalassemia. In addition, cousin marriage was prevalent in 86% of the families included in the study, underscoring the need for increased awareness and genetic counseling within these communities.

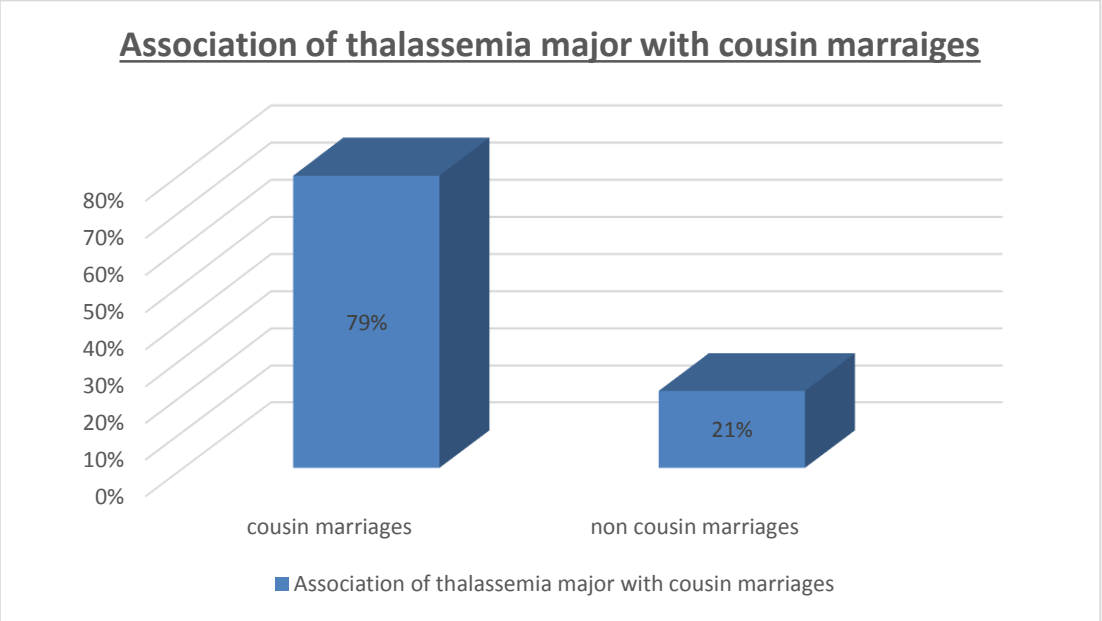


**Fig 1**: The bar graph illustrates the prevalence of cousin marriages among patients with Thalassemia major, with the x-axis representing the percentage of marriages and the y-axis depicting the categories of cousin marriage and non-cousin marriage.

**Reasons for Cousin Marriages**

When the parents of the patients were asked about the reason for their marriage with cousins, 92% gave the reason of traditional values, while in 3% of cases, the marriage with cousins was by force and 5% was because of other reasons.

These findings shed light on the complex societal factors that contribute to the prevalence of cousin marriages and the subsequent increased risk of thalassemia major in Pakistan. The overwhelming presence of traditional values as a reason for cousin marriages reflects the deep-rooted cultural norms and beliefs regarding marriage within the same family. On the other hand, the concerning revelation of forced marriages in a small percentage of cases warrants urgent attention and intervention to protect individuals from such coercive practices.

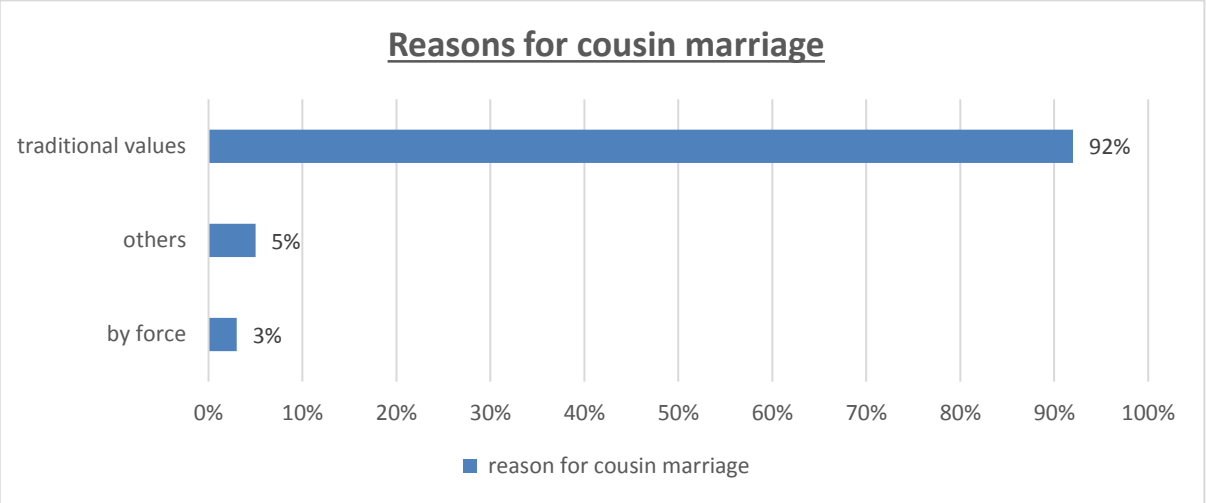


**Fig 2**: The stacked bar chart depicts the reasons provided by parents of patients with Thalassemia major for their marriage with cousins, with the x-axis representing the percentage distribution and the y-axis indicating the categories of traditional values, other reasons, and marriages by force.

**Awareness about Pre-Conception Genetic Counseling and Screening**

The survey results revealed significant gaps in awareness regarding preconception genetic counseling and screening for thalassemia. Only 7% of the study participants were aware of the availability of preconception genetic counseling and screening, while a staggering 93% had no information regarding these crucial interventions.

Furthermore, the survey highlighted the limited understanding of the genetic mode of transmission of thalassemia, as only 15% of the participants knew about its genetic inheritance and prevalence within families. This lack of awareness is concerning, as it hinders the ability of individuals to make informed decisions regarding family planning and the risk of passing on thalassemia to future generations.

Another pivotal finding was the knowledge disparity among parents of thalassemic patients, with 52% of them being aware that they were carriers of thalassemia themselves, while others did not undergo screening for it. This emphasizes the urgent need for targeted education and screening programs to identify carriers and prevent the transmission of thalassemia within families.

Inquiring about their perceptions of cousin marriages after having a thalassemic child yielded compelling insights. An overwhelming 97% of the study participants discouraged cousin marriages for their next generation, recognizing the heightened risk of genetic disorders such as thalassemia. This strong stance against cousin marriages underscores the widespread recognition of the associated health risks within the community.

However, it is noteworthy that 3% of the participants remained in favor of cousin marriages in the future despite having a child affected by thalassemia. This minority perspective underscores the complexity of societal attitudes and beliefs surrounding cousin marriages, reflecting the multifaceted nature of cultural norms and individual decision-making.

**Family History and Financial Burden**

The survey data also provided crucial insights into the financial burden and healthcare access faced by families with thalassemic children. 35% of patients had a positive extended family history of Thalassemia major, indicating the hereditary nature of the condition within families. Additionally, 24% of families had experienced deaths due to Thalassemia major, highlighting the severe consequences of this disorder.

In terms of financial implications, the survey revealed that 34% of families had a total expenditure per month ranging between Rs 4000 to 6000, while 31% incurred expenses in the range of 2000-4000 rupees. These findings underscore the significant economic strain experienced by a majority of the families, with 27% having a monthly expenditure between 6000-8000 rupees and 8% facing costs exceeding 8000 rupees. The disproportionate financial burden, especially for those with limited resources, emphasizes the urgent need for financial support and affordable healthcare options.

Moreover, 55% of the surveyed families had to visit the hospital for transfusions twice a month, and 30% visited at least once a month. This frequent need for hospital visits demonstrates the ongoing healthcare requirements and the necessity for accessible and affordable healthcare services for thalassemic patients and their families.

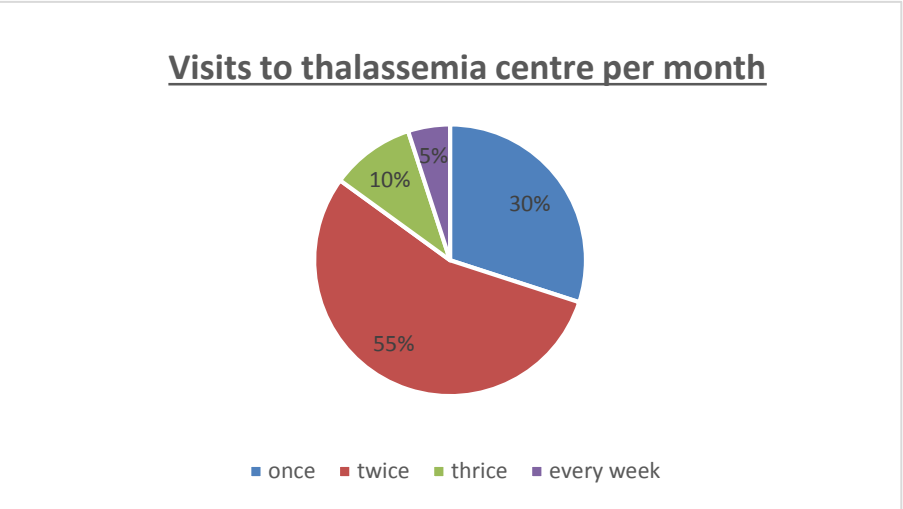


**Fig 3**. The pie chart illustrates the frequency of hospital visits per month among patients with Thalassemia, with each segment representing a different frequency category. The percentages displayed in the chart correspond to the distribution of patients based on the number of visits per month, categorized as once (30%), twice (55%), thrice (10%), and every week (5%).

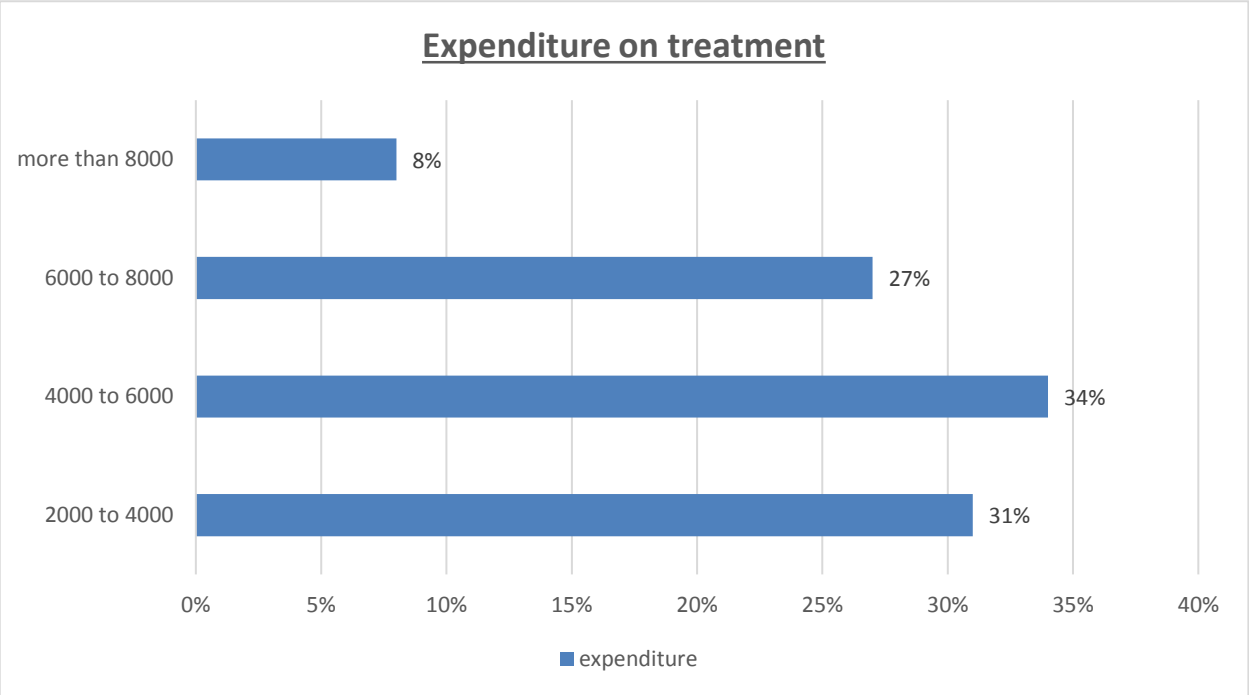


**Fig 5**: The bar graph represents the distribution of expenditure on treatment for Thalassemia patients, with the y-axis indicating the amount of money in Pakistani Rupees (PKR) and the x-axis depicting the percentage distribution. Each bar corresponds to a specific expenditure range, and the height of each bar indicates the proportion of patients with treatment expenditures falling within that range.

### Prevalence and Parental Perspectives on Thalassemia Screening and Abortion

The study revealed that 87% of parents of children with Thalassemia major expressed a desire not to continue with the pregnancy if they were informed that their child would have Thalassemia. This sentiment reflects a significant majority of parents who would opt against continuing a pregnancy in the presence of this genetic disorder. Conversely, 13% of parents indicated a preference for keeping the child despite the diagnosis of Thalassemia, highlighting a minority perspective within the study population.

## DISCUSSION

Cancer imposes a significant burden globally, affecting millions annually and resulting in substantial healthcare costs and productivity loss (18-27). Infectious diseases, on the other hand, present ongoing threats (28-26), with outbreaks like COVID-19 showcasing their potential to overwhelm healthcare systems and disrupt economies (37-45). The COVID-19 crisis has already resulted in widespread economic downturns, highlighting the vulnerability of societies to health emergencies. In Pakistan, the additional burden of thalassemia further strains healthcare resources and compounds the challenges faced by individuals and families.

Thalassemia major presents a significant genetic burden in many populations, necessitating urgent control measures to mitigate its impact. Consanguineous marriages, particularly among first cousins, significantly contribute to the prevalence of genetic disorders such as Thalassemia major (46). In our study, we observed that 86% of patients' parents confirmed cousin marriage as a prevalent custom within their families, aligning with findings from previous studies indicating high rates of consanguinity among parents of thalassemic children (47-49).

Consistent with previous research, our study found a male predominance among Thalassemia major patients (50-52). This gender disparity underscores the importance of targeted interventions and genetic counseling to address the higher susceptibility of males to the disorder. Regarding awareness and knowledge about Thalassemia major, our study revealed a concerning lack of awareness among participants, contrasting with studies conducted in other regions where higher levels of knowledge were reported (53-55). For example, a comparative study conducted in a neighboring country reported a significantly higher proportion of participants with adequate knowledge regarding the genetic mode of transmission of Thalassemia major, highlighting disparities in educational efforts and health literacy between populations (53)

The issue of abortion emerged as a sensitive topic in our study, with a significant proportion of parents expressing willingness to abort a Thalassemic fetus, despite religious and emotional considerations (50). However, a comparative study conducted in a different cultural context reported differing attitudes towards abortion in the context of Thalassemia major diagnosis, suggesting variations in cultural norms and ethical considerations surrounding reproductive choices across populations (13).

Furthermore, our study revealed a striking lack of awareness about Thalassemia major among parents prior to having an affected child, consistent with findings from other studies (13). This highlights the importance of proactive screening programs and educational initiatives to equip individuals with essential knowledge about genetic disorders and their preventive measures.

In light of these findings, legislative measures such as mandatory premarital thalassemia screening, as proposed by the government of Pakistan, are crucial for reducing the burden of Thalassemia major (56). Additionally, community-based initiatives and collaborations between government agencies, healthcare providers, and non-governmental organizations (NGOs) are essential for implementing effective prevention and control strategies, including genetic counseling and awareness campaigns (57).

## CONCLUSION

Overall, addressing the multifaceted challenges associated with Thalassemia major requires a comprehensive approach encompassing public health policies, community engagement, and education to minimize the impact of this genetic disorder on affected individuals and their families. Comparisons with findings from other studies provide valuable insights into regional variations and inform recommendations for tailored interventions to address the specific needs of diverse populations.

## REFERENCES

1. Lai K, Huang G, Su L, He Y. The prevalence of thalassemia in mainland China: Evidence from epidemiological surveys. Scientific Reports. 2017;7:920. doi:10.1038/s41598-017-00967-2.
2. Mausumi B. A study on knowledge, attitude and practice about thalassemia among the general population in the outpatient department at a tertiary care hospital of Kolkata. JPM &HH. 2015;1(1):5-12.
3. Shariq M, Moiz B, Zaidi N, et al. Pre-marital screening for β thalassemia in Pakistan: An insight. J Med Screen. 2014;21(3):163–164. doi:10.1177/0969141314532935.
4. Tazeen M, Mohammed Adil A, Ujala N, Muhammad Safwan R, Jovaria M. Frequency of β-thalassemia trait in families of thalassemia major patients, Lahore. JAMCA. 2013;25(3-4):58-60.
5. Zarei T, Razavi Z, Beiranvand R. Epidemiology of thalassemia and recent prevention and management strategies. International Journal of Hematology-Oncology and Stem Cell Research. 2019;13(3):158–167. doi:10.18502/ijhoscr.v13i3.658
6. Bittles AH. Consanguinity and its relevance to clinical genetics. Clinical Genetics.

2001;60(2):89–98. doi:10.1034/j.1399-0004.2001.600201.x

**7.** Ansari SH, Shamsi TS, Ashraf M, Bohray M, Farzana T, Khan MT, et al. Molecular epidemiology of β-thalassemia in Pakistan: Far-reaching implications. Int J Mol Epidemiol Genet. 2011;2:403–8. doi:10.1038/tpj.2014.68.

**8.** Qurat-Ul-Ain L, Laiq A, Muhammad H, Shahid MR, Farhat J. Prevalence of β-thalassemia patients associated with consanguinity and anti-HCV antibody positivity–a cross-sectional study. Pak J Zool. 2011;43(1):29-36.

**9.** Tadmouri GO, Nair P, Obeid T, Al Ali MT, Al Khaja N, Hamamy HA. Consanguinity and reproductive health problems among Arabs. Reprod Health. 2009;6:17. doi:10.1186/1742-4755-6-17.

**10.** Moiz B, Azam I, Moatter T, Hasan SH, Ali SH. Genetic counseling and prenatal diagnosis in Pakistan: Experiences and reflections from a diverse population. J Genet Couns. 2015;24(6):976–984. doi:10.1007/s10897-015-9840-4.

**11.** Saeed U, Piracha ZZ. Thalassemia: Impact of consanguineous marriages on most prevalent monogenic disorders of humans. Asian Pacific Journal of Tropical Disease. 2016;6(10):837–840. doi:10.1016/j.apjtb.2016.08.001.

**12.** Kanaan ZM, Mahfouz R, Tamim H. The prevalence of consanguineous marriage in an underserved area in Lebanon and its association with congenital anomalies. Genet Test. 2008;12(3):367–372. doi:10.1089/gte.2007.0101.

**13.** Alwan A, Modell B. Community control of genetic and congenital disorders. WHO Regional Office for the Eastern Mediterranean, Alexandria, Egypt. 1997.

**14.** Rafique B, Moinuddin A. Haemoglobinopathies and interfamily marriage in Pakistan. Pak Paedi J. 1991;15:123-131.

**15.** Nashwan AA, Al Qadrah A, Al Khaldi N. Challenges in the management of beta-thalassemia: A report of 23 patients. Journal of Taibah University Medical Sciences. 2019;14(2):174–179. doi:10.1016/j.jtumed.2018.12.007.

**16.** Mahato RK, Tamang MK, KC S. Psychosocial aspects of thalassemia: A systematic review of literature. Journal of Hematology & Oncology. 2019;12(1):1–10. doi:10.1186/s13045-018-0682-7.

**17.** Kocarnik JM, Compton K, Dean FE, Fu W, Gaw BL, Harvey JD, et al. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis. JAMA Oncol. 2022;8(3):420-44.

**18.** Tran KB, Lang JJ, Compton K, Xu R, Acheson AR, Henrikson HJ, et al. The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;400(10352):563-91.

**19.** Sharma R, Abbasi-Kangevari M, Abd-Rabu R, Abidi H, Abu-Gharbieh E, et al. Global, regional, and national burden of colorectal cancer and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol. 2022;7(7):627-647. doi:10.1016/S2468-1253(22)00032-5.

**20.** Alvarez EM, Force LM, Xu R, Compton K, Lu D, Henrikson HJ, et al. The global burden of adolescent and young adult cancer in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Oncol. 2022;23(1):27-52. doi:10.1016/S1470-2045(21)00361-7.

**21.** Da Cunha AR, Compton K, Xu R, Mishra R, Drangsholt MT, Antunes JLF, et al. The global, regional, and national burden of adult lip, oral, and pharyngeal cancer in 204 countries

and territories: A systematic analysis for the global burden of disease. JAMA Oncol. 2023;9(10):1401-1416. doi:10.1001/jamaoncol.2022.7021.

**22.** Nejadghaderi SA, Moghaddam SS, Azadnajafabad S, Rezaei N, et al. Burden of thyroid cancer in North Africa and Middle East 1990–2019. Front Oncol. 2022;12:955358. doi:10.3389/fonc.2022.955358.

**23.** Abbasi-Kangevari M, Moghaddam SS, Ghamari SH, et al. The burden of prostate cancer in North Africa and Middle East, 1990–2019: Findings from the global burden of disease study. Front Oncol. 2022;12:961086. doi:10.3389/fonc.2022.961086.

**24.** Azadnajafabad S, Moghaddam SS, Mohammadi E, Rezaei N, et al. Burden of breast cancer and attributable risk factors in the North Africa and Middle East region, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Front Oncol. 2023;13:1132816. doi:10.3389/fonc.2023.1132816.

**25.** Piracha ZZ, Saeed U. Leucine-rich repeats and immunoglobulin-like domains protein 1 (LRIG1) is downregulated in Invasive ductal carcinoma and potential prognostic marker of breast cancer. J Cancer Res Ther.

**26.** Collaborative R, Zaborowski AM, Abdile A, Adamina M, Aigner F, et al. Characteristics of early-onset vs late-onset colorectal cancer: a review. JAMA Surg. 2021;156(9):865-874. doi:10.1001/jamasurg.2021.3660.

**27.** Ikuta KS, Swetschinski LR, Aguilar GR, Sharara F, Mestrovic T, Gray AP, et al. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;400(10369):2221-48. doi:10.1016/S0140-6736(22)01944-4.

**28.** Blach S, Terrault NA, Tacke F, Gamkrelidze I, Craxi A, Tanaka J, et al. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. Lancet Gastroenterol Hepatol. 2022;7(5):396-415. doi:10.1016/S2468-1253(21)00468-4.

**29.** Sheena BS, Hiebert L, Han H, Ippolito H, Abbasi-Kangevari M, et al. Global, regional, and national burden of hepatitis B, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol. 2022;7(9):796-829. doi:10.1016/S2468-1253(22)00220-4.

**30.** Azhar A, Saeed U, Piracha ZZ, Amjad A, Ahmed A, Batool SI, et al. SARS-CoV-2 related HIV, HBV, RSV, VZV, Enteric viruses, Influenza, DENV, S. aureus and TB co-infections. Arch Pathol Clin Res. 2021;5(1):026-033. doi:10.15436/2381-1964.21.392.

**31.** Piracha ZZ, Saeed U. Global emergence of Langya virus: A serious public health concern. J Global Health. 2023;13.

**32.** Piracha ZZ, Saeed U, Tariq MN, Gilani SS, Rauf M, Ghyas H, et al. Emerging One Health Preparedness to Combat National Burden of Diseases in Pakistan: A Comprehensive Insight. J Community Med Health Sol. 2023;4(2):080-088. doi:10.15436/2381-1964.23.279.

**33.** Piracha ZZ, Tariq MN, Rasool M, Gilani SS, Saeed U, Rana MSF, et al. Catalyzing Global Action: Addressing SARS-CoV-2 Vaccine Hesitancy, Knowledge Disparities, and Epidemic Preparedness Challenges in Pakistan. Biomed J Sci & Tech Res. 2022;52(3):43702-43707. doi:10.26717/BJSTR.2022.52.004349.

**34.** Uppal SR, Uppal R, Khan AA, Saeed U, Piracha ZZ, Ali Z. Estimating the Prevalence of Fungal Nail Infections and Potential Concerns for Central Disease Surveillance Hub in Pakistan. Arch Clin Biomed Res. 2022;6(3):462-465. doi:10.15436/2381-1964.22.362.

**35.** Uppal SR, Khan AA, Uppal R, Saeed U, Piracha ZZ, Uppal R. Rising Surge of Antimicrobial Resistance and Urinary Tract Infections in Pakistani Children: A Potential Life-Threatening Scenario. Fortune J Health Sci. 2022;5(2):281-283. doi:10.15436/2381-1964.22.290.

**36.** Micah AE, Bhangdia K, Cogswell IE, Lasher D, Lidral-Porter B, et al. Global investments in pandemic preparedness and COVID-19: development assistance and domestic spending on health between 1990 and 2026. Lancet Global Health. 2023;11(3):e385-e413. doi:10.1016/S2214-109X(22)00527-7.

**37.** Saeed U, Piracha ZZ, Uppal SR, Waheed Y, Uppal R. SARS-CoV-2 induced hepatic injuries and liver complications. Front Cell Infect Microbiol. 2022;12:726263. doi:10.3389/fcimb.2022.726263.

**38.** Saeed U, Piracha ZZ, Uppal R, Uppal R. SARS-CoV-2-Associated CRP, DD, FER, HBA1c, IL6, LDH, PBNP, and PCT biomarkers and high-resolution computed tomography during the first three waves of COVID-19 in Pakistan (2019…). Jundishapur J Microbiol. 2023;15(1).

**39.** Saeed U, Piracha ZZ, Uppal R, Khan AA, Rasheed A, Waheed A, et al. Evaluation of SARS-CoV-2 spike antibody levels among Sputnik V first dose vaccinated people in Pakistan: formulation of national anti-COVID-19 mass vaccination strategy. Arch Clin Biomed Res. 2023;6(01):209-216. doi:10.3390/jdb2020050.

**40.** Saeed U, Piracha ZZ, Ashraf H, Tasneem S, Uppal SR, Islam T, et al. Effectivity analysis of COVID-19 vaccines against emerging variants of SARS-CoV-2. Arch Clin Biomed Res. 2023;6(01):209-216. doi:10.3390/jdb2020050.

**41.** Saeed U, Piracha ZZ, Kanwal K, Munir M, Waseem A, Nisar T, et al. Contemplating SARS-CoV-2 infectivity with respect to ABO blood groups. Int J Clin Virol. 2023;5(2):082-086. doi:10.3390/jdb2020050.

**42.** Marghoob M, Saeed U, Piracha ZZ, Shafiq H, Fatima N, Sarfraz N, et al. SARS-CoV-2 Infection and Incidence of Mucormycosis. Arch Clin Biomed Res. 2023;6(1):41-49. doi:10.3390/jdb2020050.

**43.** Piracha ZZ, Saeed U, Sarfraz R, Asif U, Waheed Y, Raheem A, et al. Impact of SARS-CoV-2 on Onset of Diabetes and Associated Complications. Arch Clin Biomed Res. 2023;6(1):217-227. doi:10.3390/jdb2020050.

**44.** Nadeem H, Ayesha M, Saeed U, Piracha ZZ, Tahir R, Mehtab F, et al. SARS-CoV-2 infection-associated detrimental effects on the various human organs. Int J Clin Virol. 2023;5(2):072-081. doi:10.3390/jdb2020050.

**45.** Hannan H. Consanguineous marriages: Preconception consultation in primary health care settings. J Community Genet. 2012;3(3):185–192. doi:10.1007/s12687-012-0087-0.

**46.** Khalid N, Noreen K, Qureshi FM, Mahesar M. Knowledge of thalassemia and consanguinity: A multicenter hospital-based retrospective cohort study from the metropolitan city of Karachi, Pakistan. Pak Med J. 2019;35(4):868–872. doi:10.12669/pjms.35.4.457.

**47.** Sundus A, Shamaila S, Saima M. Screening of thalassemia trait in parents of beta-thalassemia major patients in district Kohat, Pakistan. Gomal Journal of Medical Sciences. 2013;11(2):242–245.

**48.** Abbasi-Kangevari M, Derakhshani S, Saeed U, Piracha ZZ, Amini E, Khan AU. Breast Cancer-Associated Immune Checkpoints and Therapeutic Implications. Curr Drug Targets. 2023;25(5):546-554. doi:10.2174/1389450140666220218103435.

**49.** Aamir U, Khan AA, Saeed U, Piracha ZZ, Uppal R, et al. Emerging new drug resistance and

therapeutic strategies against Mycobacterium tuberculosis. Antibiotics (Basel). 2022;11(6):648. doi:10.3390/antibiotics11060648.

**50.** Piracha ZZ, Saeed U, Khan AA, Uppal R, Uppal R. SARS-CoV-2-Associated Myocardial Injury and Cardiovascular Implications. Front Cardiovasc Med. 2022;8:796798. doi:10.3389/fcvm.2021.796798.

**51.** Piracha ZZ, Saeed U, Uppal R, Kanwal K, Uppal SR, et al. Evidence-based Therapeutic Options for Coronavirus Disease 2019 (COVID-19). Antibiotics (Basel). 2021;11(1):35. doi:10.3390/antibiotics11010035.

**52.** Piracha ZZ, Saeed U, Uppal R, Uppal R. A comprehensive review of pathophysiology, clinical symptoms, and therapeutic options for novel coronavirus disease 2019 (COVID-19). Antibiotics (Basel). 2021;10(9):1245. doi:10.3390/antibiotics10091245.

**53.** Piracha ZZ, Saeed U, Kanwal K, Uppal R, Uppal R. Immunology, serology, and novel therapeutic strategies for coronavirus disease 2019 (COVID-19). Antibiotics (Basel). 2021;10(10):1142. doi:10.3390/antibiotics10101142.

**54.** Piracha ZZ, Saeed U, Waheed Y, Uppal SR, Khan AA, et al. Emerging treatment strategies and drug candidates for COVID-19: A systematic review. Front Pharmacol. 2021;12:651783. doi:10.3389/fphar.2021.651783.

**55.** Piracha ZZ, Saeed U, Uppal R, Uppal R. Non-Pharmacological Treatment Strategies for COVID-19. Arch Biomed Res. 2021;7(3):234-237. doi:10.30954/2277-2426.03.2021.1.

**56.** Piracha ZZ, Saeed U, Uppal R, Uppal R. Clinical presentations, pathophysiology, and therapeutic options for COVID-19. Int J Clin Virol. 2021;5(1):010-019. doi:10.3390/ijcv5010004.

**57.** Piracha ZZ, Saeed U, Uppal R, Uppal R. Etiology, pathogenesis, clinical presentations, and treatment options for COVID-19. Int J Clin Virol. 2021;5(2):036-045. doi:10.3390/ijcv5010004.