Genodermatoses in the Gulf Countries

Khalid Al Aboud, M.D[1]
Khalid Al Hawsawi,M.D[2]
V Ramesh[3]

Abstract

Genodermatoses in the Gulf countries have been reviewed. The high occurrence of diseases like epidermolysis bullosa, mal de Meleda and biotinidase deficiency have been noted. New syndroms are also continuously being reported. Molecular studies have revealed findings different from those described elsewhere. These have been linked to the large family size and tribal customs that lead to consanguinity. Influx of immigrants, wars and environmental pollutants are likely to worsen the situation. As treatment of genetic disorders is a challenging issue, prevention must be targeted by providing good premarital counseling and altering the tribal customs that promote consanguinity.

Introduction

Of the non-communicable diseases, genetic diseases are a major cause of both morbidity and mortality. There are isolated reports on a number of genetic conditions in the Arab population. These try to unveil the complexities of inheritance in a rapidly emerging population with common cultural, historical, traditional and religious ties. The large family size, high rate of consanguinity and other permitted forms of intermarriage make the Arabs an ideal group for the study of genetically inherited diseases. Most studies have concentrated on blood disorders, the commonest ones seen in the gulf. This prompted us to review the genodermatoses seen in the region.

Genodermatoses are inherited disorders determined by chromosomal aberrations or a single gene factor.[1] As disorders due to single gene factors are common and affect many people, these dermatoses in the gulf have been reviewed to acquaint the reader with the prevailing situation. The tables list the genodermatoses reported in the states of the Gulf Cooperation Council namely, Kingdom of Saudi Arabia, United Arab Emirates, Kuwait, Sultanate of Oman, Kingdom of Bahrain and Qatar. Yemen has recently entered this conglomerate and the article includes mainly those Yemenis working in the gulf states other than Yemen.

The diseases have been categorized, where possible, according to the predominant cutaneous manifestation. The rest have been placed in the last group. For ease of reference, the online version of Mendelian inheritance in man (OMIM) numbers are given for each disease which can be explored at the website http://www.nebi.nlm.nih.gov/omim.

Discussion

Published data reveal that many genodermatoses have been seen in the gulf countries. Many also go unreported due to lack of manpower in peripheral areas. Patients too do not seek medical advice for non-life threatening disorders like neurofibromatosis and tuberous sclerosis that are quite frequent but undocumented. One publication[2] on genetic disorders lists 115 new genetic syndromes reported over the past two decades in Arabs. Of these, 100 syndromes are autosomal recessive, 10 are autosomal dominant, and 5 are possibly x-linked recessive or autosomal recessive. Recently, a website, regularly edited and reviewed by experts, has also been established[3] with more than a thousand entries providing information in a specific population and can be reached at www.agddb.org.

Genetically inherited diseases in the gulf range from developmental defects giving rise to absence or partial presence of a particular part to biochemical ones that present in varied forms with systemic features. The exact nature of the defect in many still needs to be defined. Consanguinity is almost always present except in stray reports where it is either not mentioned [4] or not seen.[5-7] The high occurrence of some disorders has suggested the need for nationwide screening. Epidermolysis bullosa is one such disease whose prevalence is said to be much higher than that reported in the entire middle east and the authors recommended the need for prenatal tests to predict the severe forms.[8] Biotinidase deficiency is relatively common in Saudi Arabia, and the frequency of organic acid disorders is said to be 1 in 740 births and much more in certain tribes.[9] The same is true of cutis laxa, an unusually frequent disease, where cases with differing modes of inheritance have been seen.[10] Pterygium syndrome, a disabling disease, has been often reported from Kuwait.[11] Some like albinism have been occasionally

[1]*Dermatology Department,Dr.Bakhsh Hospital, Makkah, Saudi Arabia.*

[2]*Dermatology Department, Hera general hospital, Makkah, Saudi Arabia*

[3]*Dermatology Department,All India Institute for Medical Sciences*

Address for correspondence, Khalid Al Aboud, M.D, P.O Box 5440, Makkah, Saudi Arabia. Tel 966 2 5566411, Fax 966 25574350, E-mail amoa65@hotmail.com

reported. [12] An array of overlapping features have been seen in related syndromes namely, infantile systemic hyalinosis and juvenile systemic fibromatosis [13], gerodermia osteodysplastica and wrinkly skin syndrome[14], and reticulate acropigmentation of Kitamura and Dowling-Degos disease.[15,16]

The high incidence of inherited defects also explains the appearance of new syndromes with cutaneous abnormalities in the gulf states. They have been seen as keratinization defects and hair anomalies [17,18]; loose or lax skin and joints with other defects [19,20], or associated with known syndromes [21,22]; and along with a variety of dysmorphic features. [23,24] Some appear to be newer variants of Ehlers-Danlos syndrome [20,25] while another one has been eponymously named Teebi overgrowth syndrome.[19]

Limited studies in some conditions at the molecular level have revealed that the findings are at variance with those seen elsewhere. These include ataxia telangiectasia [26], atrichia congenita [27], autosomal recessive congenital ichthyosis [28] and autosomal recessive hypotrichosis simplex .[29] Unique mutations have been described in dyskertosis congenita [30], junctional epidermolysis bullosa [8] and mal de Meleda.[31]

Therapy :

Treatment of genodermatosis can be challenging. Though some like lethal congenital erythroderma are not compatible with life [32] , there are others where the quality of life can be improved by treatment. These are often metabolic disorders and range from mere reversal of hypopigmentation in homocystinuria with pyridoxine [33] to dramatic response in Richner Hanhart syndrome to diet restriction in tyrosine and phenylalanine.[34] Unrecognized, a condition like multiple carboxylase deficiency which responds to biotin can be fatal.[35] The advent of retinoids has also reversed the prognosis of some genodermatoses: sebaceous gland hyperplasia [36] and Papillon-Lefevre syndrome [37] are good examples and an encouraging response has been seen in harlequin ichthyosis.[38] Advanced therapy like bone marrow transplantation has been done with success in Chediak-Higashi syndrome.[39]

Conclusion :

It would be obvious from the reports that many patients are strictly not gulf citizens but hail from other countries like Sudan, Egypt, Syria, Turkey, Palestine and Pakistan. As the oil driven economy of the gulf states accelerates progress the influx would be more from other countries. Many stay for long or even settle. Wars too contribute to environmental changes that can lead to mutation. These factors are likely to add new diseases that may make their appearance later. It is difficult to intervene here but what is needed now is a programme for routinely screening the common genodermatoses and identifying those at risk. Prevention should be brought about by appropriate premarital counseling and discouraging consanguineous marriages. To effectively channelise these services to the community, a Center for Arab Genetic Studies was recently established in June 2003 in Al Wasl Hospital, Dubai, U.A.E. which can be reached at www.cags.org.ae.

References

1. *Harper J. Genetics and Genodermatoses. In: RH Champion, JL Burton, FJG Ebling, eds., Rook's Textbook of Dermatology, Oxford, Blackwell, 1992: pp 305-372*
2. *Teebi A, Farag T. Genetic disorders among Arab populations. Oxford Monographs on Medical Genetics No.30.Oxford, Oxford University Press, 1996*
3. *Teebi AS, Teebi SA, Porter CJ, Cuticchia AJ. Arab genetic disease database (AGDDB): a population specific clinical and mutation database. Hum Mutat 2002;19:615-621*
4. *Tallab T, Mourad MM, Ibrahim K. Acrodermatitis enteropathica (AE) associated with immunodeficiency. J Saudi Soc Dermatol Venereol 2002;8:27-30*
3. *Selim M, Al Abdulla HA, Al Saleh A, Azadeh B. Comel-Netherton syndrome. Case presentation with review of literature. Gulf J Dermatol Venereol 2000; 7:1-7*
6. *Al Hawsawi K, Al Aboud K, Ramesh V, Al Aboud D. Dyschromatosis universalis hereditaria: report of a case and review of the literature. Pediatr Dermatol 2002;19:523-526*
7. *Alfadley A, Al Hawsawi K, Al Aboud K. Ichthyosis follicularis: A case report and review of the literature. Pediatr Dermatol 2003;20:48-51*
8. *Nakano A, Lestringant GG, Paperna T, Bergman R, Gershoni R, Frossard P, et al. Junctional epidermolysis bullosa in the Middle East: Clincal and genetic studies in a series of consanguineous families. J Am Acad Dermatol 2002;46:510-516*
9. *Rashed M, Ozand PT, Al Aqeel , Gascon GG. Experience of King Faisal Hospital and Research Center with Saudi organic acid disorders. Brain & Dev 1994;16s:1-6*
10. *Agha A,Sakati NO, Higginbottom MC, Jones KL Jr., Bay C, Nyhan WL. Two forms of cutis laxa presenting in the newborn. Acta Paediatr Scand 1978;67:775-780*

11. *Teebi AS, Daoud AS. Multiple pterygium syndrome: a relatively common disorder among Arabs. J Med Genet 1990; 27:791*
12. *Smigura FC, Razzaq YA, Tomas MEP. Maple syrup urine disease. Saudi Med J 1988;9:646-647*
13. *Al-Thani G, Selim MM, Abdulrahman H. An overlap of infantile systemic hyalinosis and juvenile fibromatosis: a report of two sisters and affected. (and review of the literature). Gulf J Dermatol Venereol 1999; 6:11-20*
14. *Al Gazali LI, Sztriha L, Skaff F, Hass D. Gerodermia Osteodysplastica and wrinkly skin sybdrome: are they the same? Am J Med Genet 2001;101:213-220*
15. *Lestringant GG, Masouye I, Frossard PM, Adeghate E, Galadari IH. Co-existence of leukoderma with features of Dowling-Degos disease: reticulate acropigmentation of Kitamura spectrum in five unrelated patients. Dermatology 1997;195:337-343*
16. *Al Hawsawi K, Al Aboud K, Al Fadley A, Al Aboud D. Reticulate acropigmentation of Kitamura-Dowling Degos disease overlap: a case report. Int J Dermatol 2002; 41: 518-520*
17. *Alfadley A, Parkes R. Two Siblings born preterm with large ears and hypopigmented hair who developed palmoplantar keratoderma and frontal skull bossing: A new syndrome? Pediatr Dermatol 2002;19:224-228*
18. *Lestringant GG, Kuster W, Frossard PM, Happle R. Congenital ichthyosis, follicular atrophoderma, hypotrichosis and hypohidrosis: a new genodermatosis? Am J Med Genet 1998;75:186-189*
19. *Teebi AS, Sundareshan TS, Hammouri MY, Al Awadi SA, Al Saleh GA. A new autosmal recessive disorder resembling Weaver. Am J Med Genet 1989;33:479-482*
20. *Al Fadley F, Al Manea W, Nykanen DG, Al Fadley A, Bulbul Z, Al Haless Z. Severe tortuosity and stenosis of the systemic, pulmonary and coronary vessels in 12 patients with similar phenotypic features: a new syndrome? Cardiol Young 2000;10:582-589*
21. *Sabry MA, Ismail EA, Al-Naggar RL, Al-Torki NA, Farah S, Al-Awadi SA, et al. Unusual traits associated with Robinow syndrome. J Med Genet 1997;34:736-740*
22. *Moussa M, Ul-Haque A, Ahlberg A. Ehlers-Danlos syndrome associated with Ollier disease. Annal Saudi Med 1994;14:260-262*
23. *Teebi AS, Naguib KK, Al Awadi S, Al Saleh QA. New autosomal recessive faciodigitogenital syndrome. J Med Genet 1988;25:400-406*
24. *Al Gazali LI, Aziz SA, Salem F. A syndrome of short stature, mental retardation, facial dysmorphism, short webbed neck, skin changes and congenital heart disease. Clin Dysmorphol 1996;5(4):321-*
25. *Farag TI, Schimke RN. Ehlers-Danlos syndrome: a new oculo- scoliotic type with associated polyneuropathy? Clin Genet 1989;35:121-124*
26. *Joshi RK, Al Asiri RH, Haleem A, Abanmi A, Patek CK. Cutaneous granuloma with ataxia telangiectasia a case report and review of literature. Clin Exp Dermatol 1993;18:458-461*
27. *Cinchon S, Anker M, Vogt IR, Rohleder H, Putzstuck M, Hillmer A, et al. Cloning, genomic organization, alternative transcripts and mutational analysis of gene responsible for autosomal recessive universal congenital alopecia. Hum Molec Genet 1998;7:1671-1679*
28. *Krebsova A, Kuster W, Lestringant GG, Schulze B, Hinz B, Forrsard PM, et al. Identification, by homozygosity mapping, of a novel locus for autosomal recessive congenital ichthyosis on chromosome 17p, and evidence for further genetic heterogeneity. Am J Hum Genet2001;69:216-222*
29. *Betz RC, Al Aboud K, Al Hawsawi K, Al Aboud D, Al Githami A, Dewald G, Nthen MM. Molecualr genetic studis in autosomal recessive hypotrichosis simplex. 13th Annual Meeting of the Geneva Society of Human Genetics, Leipzig, Germany. Medizinische Genetik 2002:3*
30. *Safa WF, Lestringant GG, Frossard PM. X-linked dyskeratosis congenita: restrictive pulmonary disease and a novel mutation. Thorax 2001;56:891-894*
31. *Eckl KM, Stevens HP, Lestringant GG, Westenberger-Treumann M, Traupe H, Hinz B, et al. Mal de Meleda (MDM) caused by mutations in the gene for SLURP-1 in patients from Germany,Turkey, Palestine, and the United Arab Emirates. Hum Genet 2003;112:50-56*
32. *Shield JP, Judge MR, Readon W, Baraitser M, Nohria M, Malone M, et al. lethal congenital erythroderma: a newly recognized genetic disorder. Clin Genet 1992;41:273-277*
33. *Al Essa M, Rashed M, Ozand PT. Saudi experience with classical homocytinuria. Annal Saudi Med 1998;18:230-233*
34. *Al-Essa MA,Rashed MS,Ozand PT.Tyrosinaemia type II: an easily diagnosed metabolic disorder with a rewarding therapeutic response. Eastern Mediterranean Health Journal 1999;5:1204-1207*
35. *Sweetman L, Nyhan WL, Sakati NA, Ohlsson A, Mange MS, Boychuk RB, Kaye R. Organic aciduria in neonatal multiple carboxylase deificiency. J Inherit Metab Dis 1982;5:49-53*
36. *Bahamdan K, Tallab T, Mourad MM. Familial presenile sebaceous gland hyperplasia. Gulf J Dermatol Venereol 2000;7:44-46*
37. *Al Khenaizan S. Papillon-Lefevre syndrome :the response to acitretin. Int J Dermatol 2002;41:938-941*
38. *Selim MM, Al Bou-Ainain HH, Al Ansari H. Harlequin icthyosis. Gulf J Dermotol Venereol 2000;7:1-9*
39. *Islam AM, Hawsawi ZM, Islam M, Ibrahim O. Chediak-Higashi syndrome: an accelerated phase with hereditary elliptocytosis: case report and review of the literature. Ann Saudi Med 2001;21:221-224*
40. *Selim MM, Al Thani G, Al Abdulla H A, Azadeh B, Al Mahmoud B, Azzam A. Anhidrotic or hypohidrotic ectodermal dysplasia. Gulf J Dermatol Venereol 2001;8:2-13*
41. *Al Hawsawi K, Al Aboud K, Alfadley A, Al Aboud D. Anonychia congenita totalis: a case report and review of the literature. Int J Dermatol 2002; 41:397-399*

42. Kenue RK, Al Dhafri KS, Isolated congenital atrichia in an Omani kindred. Dermatology 1994;188:72-7

43. Al Ghamdy A. Atrichia congenita. Proceedings of 7th National Symposium of Saudi Society of Dermatology and Venereology, Gizan, 2001, p24

44. Reddy DV, Madenlioglu M. Chondroectodermal dysplasia (Ellis-van (Creveld Syndrome): report of two cases from Saudi Arabia. Clin Pediatr 1967;6:51-56

45. Benjamin B, Omojola MF, Ashouri K. Clinical and radiological features of chondroectodermal dysplasia. Ann Saudi Med 1991;11:534-538

46. Al Gazali LI, Dawodu AH, Hamada M, Bakir M, Bakalinova D. Severe facial clefting, limbic dermoid, hypoplasia of the corpus callosum, and multiple skin appendages: severe frontofacionasal "dysplasia" or newly recognized syndrome? Am J Med Genet 1996;36:346-347

47. Al Aboud K, Al Hawsawi K, Al Aboud D, Al Githami A. Hereditary hypotrichosis simplex: report of a family. Clin Exp Dermatol 2002; 27;654-656

48. Galadari I, Mohsen S. Leukonychia totalis associated with kertosis pilaris and hyperhidrosis. Int J Dermatol 1993; 32:524-525

49. Al Awadi SA, Farag TI, Teebi AS, Naguib K, el-Khalifa MY, Kelani Y, et al. Primary hypogonadism and partial alopecia in three sibs with mullerian hypoplasia in the affected females. Am J Med Genet 1985;22:619-622

50. Al Jurayyan NA, Al Mugeiren MM, Al Nasser MN, Boohene A. Vitamin D resistant rickets and alopecia in a Saudi Child. Saudi Med J 1992;13:159-162

51. Al Anzy HM, Alsaleh QA, Salem MT, Nadi H, Sameer E. A new variant of of 1,25-dihydroxyvitamin D-receptor-defect rickets and alopecia. Associated with mental retardation and hearing loss. Gulf J Dermatol Venereol 1998;5:30-31

52. Woodhouse NJ, Sakati NA. A syndrome of hypogonadism, alopecia, diabetes mellitus, mental retardation, deafness and ECG abnormalities. J Med Genet 1983;20:216-219

53. Gul D, Ozata M, Mergen H, Odabasi Z, Mergen M. Woodhouse and Sakati syndrome (MIM 241080): report of a new patient. Clin Dysmorphol 2000; 9200:123-125

54. Al Shahrani D, Al Dowaish A. What's your diagnosis. Ann Saudi Med 1999;19:141-143

55. Al Nozha MM, Niazi M, Al Khairy KS. Fanconi's anaemia presenting as Myelodysplastic syndrome in association with pseudo-Gaucher cells in the bone marrow. Saudi Med J 1989;10:411-414

56. Selim MM, Al Saad T, Abu M. Incontinentia Pigmenti (Bloch Sulzberger Syndrome)(Bloch-Siemen's Syndrome). Gulf J Dermatol Venereol 1999;6:52-55

57. Al Khenaizan S. Incontinentia pigmenti. Annal Saudi Med 2000; 20:424-426

58. Meshikhes AN. Peutz-Jeghers syndrome: associated with cancer and surgical managment. Annal Saudi Med 2000; 20:413-414

59. Selim MM, Al Mahmoud B. Piebaldism- report of three cases and review of the literature. Gulf J Dermatol Venereol 2000; 7:22-25

60. Alfadley A, Al-Ajlan A, Hainu B, Pederson KT, Al Hoqail I. Reticulate acropigmentation of Dohi: A case report of autosomal recessive inheritance. J Am Acad Dermatol 2000; 43:113-117

61. Lestringant GG, Aal GA, Frossard PM, Qayed KI. Recticulate acropigmentation of Kitamura: Pigment specks and pits in unusual locations. Br J Dermatol 1994;131:137-139

62. Al Qahtani F, Salloum A. Chanarin-Dorfman syndrome: a case report. Annal Saudi Med 2002; 22:354-355

63. Barr DG,Kirk JM,al Howasi M,Wanders RJ,Schutgens RB.Rhizomelic chondrodysplasia punctata with isolated DHAP-AT deficiency. Arch Dis Child 1993;68:415-417

64. Sztriha L, Al-Gazali LI, Wanders RJ, Ofman R, Nork M, Lestringant GG. Abnormal myelin formation in rhizomelic chondrodysplasia punctata type 2 (DHAPAT – deficiency). Dev Med Child Neurol 2000;42:492-495

65. Mysore V, Al Suwaid A. Icthyosis bullosa of Siemens, a case report. Gulf J Dermatol Venereol 2000; 7:32-33

66. Senter TP, Jones KL, Sakati N, Nyhan WL. A typical ichthyosiform erythroderma and congenital neurosensory deafness – a distinct syndrome. J Pediatr 1978;92:68-72

67. Joshi RK, Singh B, Al Shahwan SA, Abanmi A. The Sjogren Larsson Syndrome: An inborn error in the fatty alcohol cycle. Saudi Med J 1995;16:61-63

68. Al Jasmi F, Al Khenaizan S. X-linked ichthyosis and undescended testes. Int J Dermatol 2002;41:614-616

69. Ismail EA, Dillon MJ, Shafik MH, Youssef TM. Chronic infantile neurological cutaneous articular syndrome in an Arab Patient. Pediatr Int 2001; 43:514-516

70. Galadari I, Aal AJ. Epidermodysplasia verruciformis: report of a case with palmar pits. Cutis 1993:52:53-55

71. Kamal AA, Azadeh B, Al Saleh A, Selim MM. Multiple trichoepithelioma, a review and report of a case showing unusual findings. (A new syndrome). Gulf J Dermatol Venereol 1999;6:17-25

72. Raddadi AA, Al Twaim AA. Type A Niemann-Pick disease. J Euro Acad Dermatol Venereol 2000;14:301-303

73. Al Homrany M, Tallab T, Bahamdan K A, Khare Ak, Ugere JU, Mourad MM. Darier-White disease in a Saudi patient associated with systemic involvement. Afr J Med Sci 1997; 26:195-196

74. Alsaleh QA, Teebi AS. Autosomal recessive epidermolytic palmoplantar keratoderma. J Med Genet 1990;27:519-522

75. Alfadley A, Al Hawsawi K, Hainau B, Al Aboud K. Two brothers with keratosis follicularis spinulosa decalvans. J Am Acad Dermatol 2002;47: S275-278

76. Lestringant GG, Halawani NA, Zagzouk F. Mal de Meleda. Int J Dermatol 1989;28:277-78

77. Lestringant GG, Hadi SM, Qayed KI, Diayney BJ. Mal de Meleda: recessive transgressive palmoplantar keratoderma with three unusual facultative features. Dermatology 1992;184:78-82

78. *Lestringant GG, Frossard PM, Adeghate E, Qayed KI. Mal de Meleda: a report of four cases from United Arab Emirates. Pediatr Dermatol 1997;14:186-191*

79. *Lestringant GG, Frossard PM, Eckl K-M, Reis A, Hennies HC: Genetic and Clinical heterogeneity in transgressive palmoplantar keratoderma. J Invest Dermatol 2001;116:825-827*

80. *Pareek SS. Papillon-Lefevre syndrome: case report .Saudi Med J 1983;4:136-138*

81. *Ullbro C. Crossner CG, Nederfors T, Al Fadley A, Pederson KT. Dermatologic and oral findings in a cohort of 47 patients with Papillon-Lefevre syndrome. J Am Acad Dermatol 2003;48:345-351*

82. *Almuneef M, Al Khenaizan S,Al Ajaji S,Al-Anazi. Pyogenic liver abscess and Papillon-Lefevre syndrome:not a rare association. Pediatrics 2003;111:e85-88*

83. *Lestringant GG, Berge T. Porokeratosis punctata palmaris et plantaris. A new entity? Arch Dermatol 1989;125:816-819*

84. *Tallab TM. Richner-Hanhart Syndrome: importance of early diagnosis and early intervention. J Am Acad Dermatol 1996;35:857-859*

85. *Reisner SH, Seelenfreund M, Ben-Bassat M. Cutis laxa associated with severe intrauterine growth retardation and congenital dislocation of the hip. Acta Paediat Scand 1971;60:357-360*

86. *Sakati NO, Nyhan WL, Shear CS, Kattan H, Akhtar M, Bay C, et al. Syndrome of cutis laxa, ligamentous laxity, and delayed development .Pediatrics 1983;72:850-856*

87. *Allanson J, Austin W, Hecht F. Congenital cutis laxa with retardation of growth and motor development: a recessive disorder of connective tissue with male lethality. Clin Genet 1986;29:133-136*

88. *Watts HG. Management of dislocated hip in patients with Fittke-type Congenital cutis laxa. Ann Saudi Med 1990;10:291-292*

89. *Farag TI, Schimke RN. Ehlers-DAnlos syndrome: a new oculo-scoliotic type with associated polyneuropathy. Clin Genet 1989;35:121-124*

90. *Abdul Jabbar A. Ehlers-Danlos Syndrome type IV associated with arterial and bowel perforation. Annal Saudi Med 2000; 20:421-423*

91. *Hunter AGW. Is gerodermn osteodysplastica underdiagnosed? J Med Genet 1988;25:854-857*

92. *Torki NA, Al Awadi SA, Cindro-Heberie L, Sabry MA. Gerodermia Osteodysplastica in a Bedouin sibship: further delineation of the syndrome. Clin Dysmorphol 1997;6:51-55*

93. *Mahajan S, Mistry M, George ND, Shivram M. Pseudoxanthoma elasticum (PXE). Gulf J Dermatol Venereol 2000; 7:53-54*

94. *Joshi RK, Atukorala DN, Abanmi A, Kudwah A. Dyskeratosis congenital in a female. Br J Dermatol 1994;130:520-522*

95. *Al Aboud K, Al Hawsawi K, Al Aboud D, Al Githami A. Kindler Syndrome in a Saudi kindred. Clin Exp Dermatol 2002; 27:673-676*

96. *Rashed MS, Rahbeeni Z, Ozand PT. Screening blood spots for arginosuccinase deficiency by electrospray tandem mass spectroscopy. Southeast Asian J Trop Med Pub Hlth 1999;30s:170-173*

97. *Pomponio RJ, Ozand PT, Al Essa M, Wolf B. Novel mutations in children with profound biotinidase deficiency from Saudi Arabia. J Inherit Metab Dis 2000; 23:185-187*

98. *Joshi S,Al-Essa Ma,Archibald A,Ozand P.T.Biotinidase deficiency:a treatable genetic disorder in the Saudi population.Eastern Mediterranean Health Journal 1999;5:1213-1217*

99. *Ozand PT, Rashed M, Millington DS, Sakati N, Hazzaa S, Rahbeeni Z, et al. Ethylmalonic aciduria: an organic acidemia with CNS involvement and vasculopathy. Brain Dev 1994;16s:12-22*

100. *Ismail EA, Al Saleh QA, Zaki M, Rao A, Sonbati S, Moosa A. The association of cystic fibrosis with Homocystinuria in two Saudi Siblings. Eur J Pediatr 1996;155:831*

101. *Harrison DA, Mullaney PB, Mesfer SA, Awad AH, Dhindsa H. management of ophthalmic complications of homocystinuria. Ophthalmology 1998;105:1886-1890*

102. *Nanda A, Alsaleh QA, Al Sabah H, Ali AM A, Anim JT. Lipoid proteinosis: Report of four siblings and brief review of the literature. Pediatr Dermatol 2001; 18:21-26*

103 *Hamada T, McLean WH, Ramsay M, Ashton GH, Nanda A, Jenkins T, et al. Lipoid proteinosis maps to Iq21 and is caused by mutations in the extracellular matrix protein 1 gene (ECM1). Hum*

104. *Mol Genet 2002;11:833-840*

Uthman MAE, Satti MB, Baraka ME. Lipoid proteinosis: Clinical, genetic and pathological study of a Saudi Arabian family. Ann Saudi Med 1991;11:418-423

105. *Mohammad AM.Maple syrup urine disease in Bahrain. Bahrain Med Bull 1985;7:114-117*

106. *O'Connell JP, Hardy MJ. Maple syrup urine disease in two sibling Saudi Arabs. Saudi Med J 1987;8:250-252*

107. *Ozand PT. Diagnosis of inborn errors of metabolism by tandem mass spectrometry. Ann Saudi Med 1998; 18:234-235*

108. *Teebi AS, Al Awadi SA, Farag TI, Naguib KK, El-Khalifa MY. Phenylketuria in Kuwait and Arab countries. Eur J Pediatr 1987;146:59-60*

109. *Jan MY, Humeida AK, Al Kuwaity KK. Report of two cases of*

acrodermatitis enteropathica. In: Mahgoub E, ed. Proceedings 5th Saudi Medical Meeting, 1980:429-440

110. *Roy D, Noor S, Mousa F, Adam KA. Acrodermatitis enteropathica. Saudi Med J 1999;20:116-119*

111. *Al Hammouri MY, Al Rashied AA, Al Mazidi Z, Al Saleht Congenital erythropoietic porphyria. J Kuwait Med Assoc 1989;123:74-76*

112. *Ismail E AR, Al Shammari N, Anim JT, Moosa A. Congenital insensitivity to pain with anhidrosis: lack of eccrine sweat gland innervation confirmed. J Child Neurol 1998; 13: 243-246.*

113. Mardy S, Miura Y, Endo F, Matsuda I, Sztriha L, Frossard P, Moosa A, Ismail E AR, Macaya A, Andria G, Toscano E, Gibson W, Graham GE, Indo Y. Congenital insensitivity to pain with anhidrosis: novel mutations in the TRKA (NTRK1) gene encoding a high affinity receptor for nerve growth factor. Am J Hum Genet 1999;64:1570-1579.

114. Sztriha L,Lestringant GG,Hertecant J,Frossard PM,Masouye I.Congenital insensitivity to pain with anhidrosis. Pediatr Neurol 2001;25:63-66

115. Karkashan E, Joharji H, Al-Harbi N. Congenital insensitivity to pain in four related Saudi families. Pediatr Dermatol 2002;19:333-335

116. Al Salem AH. Familial Dercum's disease (Adiposis Dolorosa). Saudi Med J 1993;14:71-73

117. Abahussein AA, Al Zayir AA, Mostafa WZ, Okoro AN. Inherited epidermolysis bullosa. Int J Dermatol 1993;32:730-732

118. Abahussein AA, al-Zayir AA, Mostafa WZ, Okoro AN. Epidermolysis bullosa in the eastern province of Saudi Arabia. Int J Dermatol 1993;32:579-581

119. Abanmi A, Joshi RK, Atukorala DN, Pedersen NB,Khamis OA.Autosomal recessive epidermolysis bullosa simplex.A case report. Br J Dermatol 1994;130:115-117

120. Haque KN, Al Nozha MM. Berardinelli lipodystrophy(generalized lipodystrophy syndrome): a case report and review of the literature. Ann Saudi Med 1991;12:400-402

121. El Harith EA, Al Kharasani M, Ahmed M, Stuhrmann M. hereditary hemorrhagic telangiectasia: a case report. Saudi Med J 1999;20:797-799

122. Mardini MK, Ghandour M, Sakati NA, Nyhan WL. Johanson-Blizzard syndrome in a large inbred kindred with three involved members. Clin Genet 1978;14:247-250

123. Sweetman L, Nyhan WL, Sakati NA, Ohlsson A, Mange MS, Boychuk RB, Kaye R. Organic aciduria in neonatal multiple carboxylase deficiency. J Inherit Metab Dis 1982;5:49-53

124. Cardoso E, Sundararajan M. The naevoid basal cell carcinoma syndrome. Saudi Med J 1985;6:272-276

125. Alsaad S, Redha E, Alhassan A. Delleman syndrome:a known case with an unusual finding. Kuwait Med J 2003;35:53-54

126. Abdel-Hafez K, Safer AM, Selim MM, Rehak A. Familial continual skin peeling. Dermatologica 1983;166:23-31

127. Karrar ZA, Elidrissy ATH, Al Arabi K, Adam KA.The wrinkly skin syndrome: a report of two siblings from Saudi Arabia. Clin Genet 1983;23:308-310

128. Okrasinski H. Xeroderma pigmentosum: two cases. Saudi Med J 1984;5:443-446

129. Fathy S, Khafagy H. Xeroderma pigmentosum in Qatar. Cutis 1986;37:377-379

Table 1 : Genodermatoses in the Gulf

S.No	Disorder/Phenotype	No. of patient(s) & Nationality	OMIM No.	Inheritance*	Clinical Cutaneous	Features*Other anomalies/ Systems affected
A	APPENDAGEAL LOSS					
1	Anhidrotic ectodermal dysplasia [40]	6 Qatar, Sudan, Palestine	129490 224900	AD or AR**	Absent or diminished sweat & hypotrichosis	Dental
2	Anonychia congenita simplex [41]	1	206800	AD, AR or sporadic	Absence of nails	None
3	Atrichia congenita [27,42,43]	3 Saudi Many Oman	203655	AR	Total absence of hairs Keratin cysts on face & limbs[43]	None
4	Chondroectodermal dysplasia (Ellis-van Creveld syndrome) [44,45]	3Yemen and Saudi families	209500	AR	Hypoplastic nails	Dwarfism, Teeth, Cardiac defects in 50%
5	Frontofacionasal dysplasia [46]	1UAE***	225500	AR	Hypoplasia of multiple skin appendages	Multiple facial defects, CNS+

6	Hereditary hypotrichosis simplex [47]	4 Saudi	229400 146520	AD	Progressive hair loss leading to baldness by age of 30	None
7	Leuconychia totalis [48]	1UAE	151600	AD, AR	White nails Hyperhidrosis	None
8	Primary hypogonadism and partial alopecia [49]	3Kuwait	Not available	AR	Alopecia	Hypogonadism
9	Vitamin D resistant rickets type II with alopecia [50,51]	4KuwaitSaudi	Not listed	AR	Alopecia	Rickets
10	Woodhouse & Sakati syndrome [52,53]	6Saudi	241080	AR	Alopecia	Hypogonadism Diabetes mellitus Mental retardation Deafness
B	PIGMENTARY CHANGES					
1	Chediak-Higashi syndrome [39,54]	7 Saudi	214500	AR	Albinism	Eyes
2	Dyschromatosis universalis hereditaria [6]	1Saudi	127500	AR	Leukomela noderma	None
3	Fanconi's anemia [55]	1Saudi	227650	AR	Pigmentary changes	Bone marrow Heart Kidneys Malformed limbs
4	Incontinentia pigmenti [56,57]	4QatarSaudi	308300	X-linked dominant	Typical hyperpig mentation	CNS Skeletal, Eyes, Teeth
5	Peutz-Jegher's syndrome [58]	1Saudi	175200	AD	Acral melanosis	Gastrointestinal tract
6	Piebaldism [59]	3Qatar	17280	AD	White patches on skin and scalp	None
7	Reticulate pigmentation of Dohi [60]	3 (AR)	127400	AD, rarely AR	Acral localized pigmentation	None
8	Reticulate acropigmentation of Kitamura [61]	1UAE	Not given	AD	Acral melanosis, palmar pits & no hypo pigmentation	None
C	ICHTHYOTIC SKIN					
1	Autosomal recessive congenital ichthyosis (ARCI) [28]	2UAE families	242100	AR	Variable erythema & scaling	None
2	Chanarin-Dorfman syndrome (lipid storage disease) [62]	2Saudi	275630	AR	Congenital ichthyotic erythroderma	Multiple systems