# Visual and Auditory Abnormalities in Patients with Vitiligo Vulgaris: A Case Control Study

*Thesis*

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**Dermatology**

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# ABSTRACT

**Background:** Melanocytes, the key cells in vitiligo are of neuro-ectodermal origin and exist in several organs (e.g. liver, spleen, lung, heart and brain) besides the skin. Their dysfunction in the skin occurs in vitiligo and there is controversial evidence of involvement of other sites.

**Objective:** The aim of the present work was to investigate the structure and/ or function of two of the organ systems containing melanocytes, the eyes and ears, to detect any impairment in non-segmental-vitiligo patients.

**Patients and Methods:** Sixty consecutive patients with non-segmental vitiligo fulfilling the inclusion criteria and twenty controls were the subjects of the present study. Clinical examination and VASI scoring were carried out on patients. For all subjects the following was done: 1.Fundus and slit lamp examination and electroretinogram were performed. 2. Visual evoked potentials were measured. 3. Audiometric measurements were also performed.

**Results:** The patient group was divided into those with less than 50% body surface involvement; group A (36 patients) and those with more than 50% body surface involvement group B (24 patients). Skin types of patients were III 25 pts, IV 28 pts and V 7 pts. All investigations pertaining to involvement of pigment cells in the eyes were negative invariably in all patients and controls. Auditory disturbances as evaluated by auditometry revealed non significant involvement bilaterally in seven patients and unilateral in one (15 ears) with no statistical significant difference between group A and B, and was normal in controls.

These patients were asymptomatic. The degree of hearing loss did not correlate to the extent of vitiligo or to the presence or absence of vitiligo on the face. There was a positive correlation with the disease duration.

Although there was a statistical significant difference between groups A and B regarding disease duration and VASI score, but this difference had no impact on the hearing loss, where no significant difference between the different groups was shown.

**Conclusion:** Based on the present research, in a non segmental vitiligo patient population of higher skin types of various extent and both sexes, impairment of pigment cells in the visual apparatus could not be detected. On the other hand,

auditory abnormalities are detected through audiometry in 13.3 %, without statistical significance. It is therefore of importance to guard against further otological damage by avoidance of high noise jobs and drugs with risk of oto-toxicity in these patients.

Key words:

Audiometry, Vitiligo, VEPs, ERG.

# LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| **AC** | : | Adenylate cyclase |
| **ACTH** | : | Adrenocorticotropic hormone |
| **AGRP** | : | Agouti related protein |
| **ANOVA** | : | Analysis of variants |
| **Arg160Trp (C478T)** | : | Arginine 160 Tryptophan (Cysteine478Threonine) |
| **Arg163Gln (G488A)** | : | Arginine 163 Glutamine (Glycine 488Alanine) |
| **ASIP** | : | Agouti signaling protein |
| **Asp** | : | Aspartate |
| **ATP** | : | Adenosine triphosphate |
| **BAEPs** | : | Brainstem auditory evoked potentials |
| **BB-UVB** | : | Broadband-UVB |
| **β end** | : | β Endorphin |
| **bFGF** | : | Basic fibroblastic growth factor |
| **β LPH** | : | β Lipotropic hormone |
| **cAMP** | : | Cyclic adenosine monophosphate |
| **CD** | : | Cluster of differentiation |
| **CL** | : | Cardiolipin |
| **CLA** | : | Cutaneous lymphocyte association antigen |
| **CLIP** | : | Corticotrophin like intermediate lobe |
| **CRH** | : | Corticotrophin releasing hormone |
| **Ct** | : | Cycle threshold |
| **CTLA4** | : | Cytotoxic T lymphocyte antigen 4 |
| **DAG** | : | Diacyl glycerol |
| **Db** | : | Decibels |
| **DC** | : | Dendritic cell |
| **DNA** | : | Deoxyribo nucleic acid |
| **dNTPs** | : | Deoxynucleotide triphosphate |
| **DPOAEs** | : | Distortion product otoacoustic emission |
| **DQ** | : | Dopaquinone |
| **ERG** | : | Electroretinogram |
| **ET-1** | : | Endothelin-1 |
| **GM-CSF** | : | Granulocyte monocyte colony stimulating factor |

| | | |
|---|---|---|
| **GPCRs** | : | G protein coupled receptors |
| **Gs** | : | G proteins |
| **GTC** | : | Guanidine thiocyanate |
| **GTP** | : | Guanosine 5 triphosphate |
| **H2O2** | : | Hydrogen peroxide |
| **HLA** | : | Human leucocytic antigen |
| **HPA** | : | Hypothalamic-pituitary-adrenal axis |
| **HPRI** | : | Human Placental Ribonuclease Inhibitor |
| **ICAM-1** | : | Intercellular adhesion molecule 1 |
| **IFN- γ** | : | Interferon gamma |
| **Ig** | : | Immunoglobulins |
| **IL** | : | Interleukin |
| **IP3** | : | Inositol triphosphate |
| **IQR** | : | Interquartile range |
| **K** | : | Lysine |
| **KUVA** | : | Khellin plus UVA |
| **LASER** | : | Light amplification by stimulated emission of radiation |
| **LCs** | : | Langerhans cells |
| **L-Tyr** | : | L tyrosine |
| **MCs** | : | Melanocytes |
| **MC-Rs** | : | Melanocortin receptors |
| **MHC** | : | Major histocompatibility complex |
| **MMLV** | : | Moloney murine leukemia virus |
| **mRNA** | : | Messenger Ribonucleic acid |
| **MSH** | : | Melanocyte stimulating hormone |
| **NALP1** | : | NACHT, LRR and PYD domains-containing protein 1 |
| **NB-UVB** | : | Narrow band-UVB |
| **NGF** | : | Nerve growth factor |
| **NK** | : | Natural killer cell |
| **NSV** | : | Non-segmental vitiligo |
| **NT** | : | N terminal |
| **PACE4** | : | Paired basic amino acid residue cleaving enzyme 4 |
| **PCR** | : | Polymerase Chain Reaction |
| **PCs** | : | Prohormone convertases |
| **PKC** | : | Protein kinase C |
| **POMC** | : | Proopiomelanocortin |

| | | |
|---|---|---|
| **PTA** | : | Pure tone audiometry |
| **PTPN22** | : | Protein tyrosine phosphatase, non-receptor type 22 |
| **PUVA** | : | Psoralens plus UVA |
| **qPCR** | : | Quantitative real time polymerase chain reaction |
| **R** | : | Arginine |
| **RNase** | : | Ribonuclease |
| **ROS** | : | Reactive oxygen species |
| **RQ** | : | Relative Quantification |
| **SD** | : | Standard deviation |
| **SV** | : | Segmental vitiligo |
| **Tase** | : | tyrosinase |
| **TGF-β** | : | Transforming growth factor beta |
| **Th** | : | T helper |
| **TNF-α** | : | Tumor necrosis factor alpha |
| **T Regs** | : | T regulatory cells |
| **TRP** | : | Tyrosinase related protein |
| **UV** | : | Ultra violet |
| **UVR** | : | Ultraviolet radiation |
| **VASI** | : | Vitiligo Area and Severity Index |
| **VEPs** | : | Visual evoked potentials |
| **6BH4** | : | (6R)-L-erythro-5,6,7,8,-tetrahydrobiopterin |

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# INTRODUCTION

Vitiligo is an acquired, progressive, multifactorial, depigmenting disorder characterized by the appearance of circumscribed white macules or patches in the skin and/or mucous membranes due to progressive loss of functional melanocytes in the epidermis ***(Guerra et al., 2010).*** It affects 1–2% of the population worldwide, with no predilection for gender or race, and usually starts in childhood or young adulthood ***(Kakourou, 2009).***

Embryonically, human melanocytes develop from the neural crest, later become distributed in the epidermis, hair bulbs of the skin, the uveal tract, the retinal pigment epithelium, the inner ear, and the leptomeninges, which are collectively regarded as melanocyte organs ***(Goldgeier et al., 1984).***

Retinal, iris and ciliary pigment epithelial cells are derived from the neural ectoderm, more specifically from the extremity of the embryonic optical cup, which is also the origin of the retina. In contrast, the pigment-generating cells in the choroid and in the stroma of the iris and ciliary body, uveal melanocytes, are developed from the neural crest, the same origin as the melanocytes in skin and hair ***(Hu et al., 2008).***

Although the color of the iris do not change in patients with even extensive vitiligo, depigmented areas in the pigment epithelium and choroid occur in up to 40% of patients ***(Albert et al., 1983).*** Moreover, the incidence of uveitis in patients with vitiligo is elevated, and the

incidence of vitiligo in patients with uveitis is also higher than expected ***(Wagoner et al., 1983).***

The visual evoked potentials (VEPs) represent electrical activity of large populations of neurons in the visual cortex. They test the function of the visual pathway from the retina to the occipital cortex and measure the conduction of the visual pathways from the optic nerve, optic chiasm, and optic radiations to the occipital cortex and its excitability ***(Odom et al., 2004).***

Electroretinogram (ERG) is a mass potential, which reflects the summed electrical activity of the retina ***(Marmor et al., 2009).*** ERG provides an objective, quantitative measure of retinal function and allows the clinician to monitor the function of rod cells, cone cells, and ganglion cells in each eye. It uses electrodes placed on the cornea or adjacent to the orbit to monitor changes in the electrical potential of the eye in response to specific stimuli. Careful manipulation of the stimulus and testing conditions allows the clinician to investigate different cell types and layers of the retina ***(Burns and Baylor, 2001).***

The presence of otic melanocytes was first described by AlphonseCorti in 1831***(Angrisani et al., 2009).*** These cells are primarly located throughout the stria vascularis and modiolus of the cochlea, but they also exist in the vestibular organs ***(Nordlund et al., 2006).*** Melanocytes may have an important role in the inner ear as hearing is affected in systemic disorders that affect pigmented areas such as Vogt-Koyanagi and Waardenberg Syndromes ***(Angrisani et al., 2009).***The presence of abnormalities in melanocytes is not limited to the peripheral

auditory system but also have been found in the brain stem in patients with pigment disorders ***(Ardie et al., 1998).***

Pure-tone audiometry is the main test for the diagnosis of hearing loss. It can be achieved by using either air conduction (with headphones or loudspeakers) or bone conduction (by placing a vibrator on the mastoid bone behind the ear) ***(Paquiera, Koehla and Jantzemb, 2012).***

# AIM OF THE WORK

The aim of the present work was to investigate the structure and/ or function of two of the organ systems containing melanocytes, the eyes and ears, to detect any impairment in non-segmental-vitiligo patients.