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Down's Syndrome, An Emerging Threat

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ABSTRACT

Background: Down Syndrome has been one of the emerging threats in current society with high prevalence rate of around 3000-5000 annual birth. This requires a screening and analysis of the aetiologies and other pathophysiological factors leading to the increase in current scenario.

Objective:

- To find out the root cause of Down Syndrome
- To ruled out the exact cause how oxidative stress impact in Down syndrome
- To ruled out the exact cause how delayed pregnancy or advanced age of pregnancy impact in Down Syndrome

Materials & Methods: This research has been based on the approach of mixed research methodology following interpretivism and positivism research philosophy where set of different families have been selected to isolate the changes evident within them for the pathogenesis of Down syndrome

Results: It has been found that the evidence of trisomy is the evident feature and not the actual cause where generation of oxidative stress among the families as well as multi-factorial pathways regulate the pathophysiology

Conclusion: Hence, considering the basic family pathology and maintaining appropriate psychophysiological correlation among the family-society could reduce the increasing threat in generation of Down Syndrome among foetus.

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KEYWORDS: *Down Syndrome, Trisomoy, HCR, Threat, Pathogenesis*

INTRODUCTION

The 21st century has been marked with the out-bursting changes in the pathological consequences where genetic and neuropathologies. The modern civilisation as well as busy lifestyle is responsible for the occurrence of many pathological conditions, among which some are potentially life threatening also. Thus, life has not only a materialistic subject to study; rather it has been an unrevealed truth of nature, among which human life is most complicated one to understand. Similarly, maintenance of health has been the only goal to reach for the betterment of nature where avoidance of disease or any kind of damaging influence needs to be elicited effectively. In nexus with this, the current epidemiological status of the genetic diseases such as the Down Syndrome has been increasing with the increase in the materialism of the world. For instance, the United Nation has identified that around 1 in every 1000 live births has been affected by the Down Syndrome increasing the overall prevalence by 3000-5000 child born annually. On the other hand, in India. Nearly 30,000-50,000 children born have been found affected by the Down Syndrome. Although, this has been one of the emerging threats in the near world; study related to focus on effective management as well as evaluating its aetiology has been neglected from scientific scenario. This has hence, changed the viewpoint for need of evaluating the exact scenario of down syndrome among the foetal development.

Down syndrome has been marked with the presence of supernumerary chromosome 21 that results in a collection of clinical features that are compatible with human survival post-term, and the most frequent survivable autosomal aneuploidy. The first description of a child who presumably had Down Syndrome was provided by Esquirol in 1838 where 8 years later Seguin described a patient that had similar

features suggestive of an anomaly hat later became known as Down's Syndrome. Similarly, Down syndrome has been the most common genomic disorder of intellectual disability as well as caused by the trisomy of *Homo sapiens* chromosome 21 (HAS 21). Furthermore, it has been evident that individuals with trisomy 21 present with a distinct collection of symptoms and manifestation that affect multiple body systems, although variation exists between individuals such as children affected with DS are generally of short stature, with short fingers, hypotonia, and atlantoaxial instability. Apart from this, facial characteristics generally include the presence of epicanthic folds, flat nasal bridge, and occiput, small mouth and ears, and up-slanting palpebral fissures. CHD (Congenital heart defects) are common, particularly atrioventricular septal defect and many more.

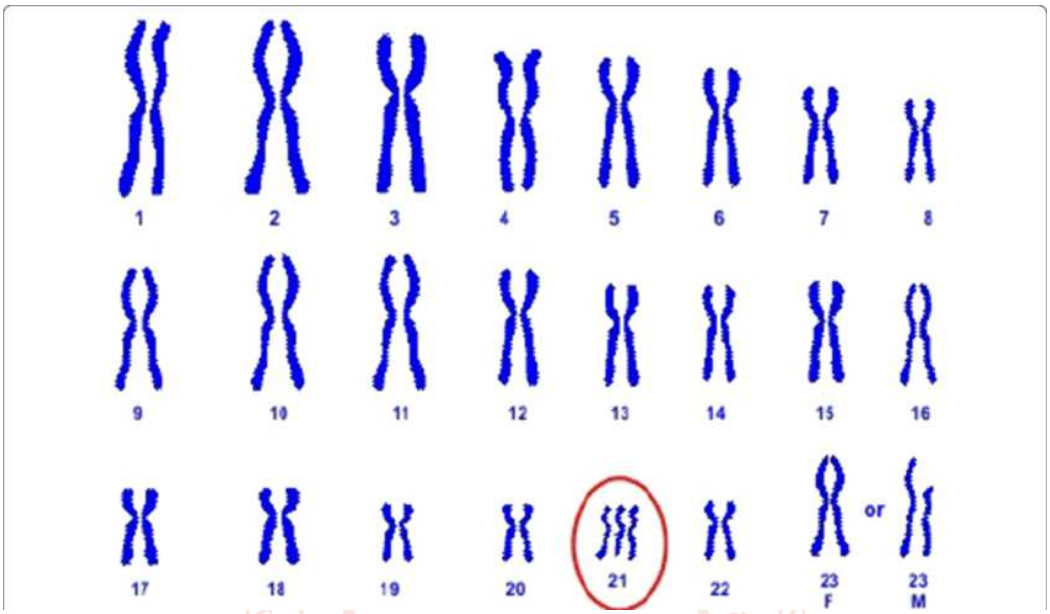

Figure 1:Karyotyping of Trisomy for Down Syndrome

From the above figure, it can be isolated that the trisomy of Down Syndrome is one of the characteristic features leading to the generation of down syndrome where varied aetiological factors including mosaic formation, mother's age and psychoneurological condition and many more have been leading to the generation of such attributes. In nexus with this, the management protocol even requires current condition of mother that could appropriately maintain the balance of individual in any changes prior to the pregnancy. Similarly, the increasing findings of children suffering from Down Syndrome has been maximum that affects the overall health from birth of the child.

At birth	Infancy & Childhood	Adulthood
Structural • Dysmorphic features • Congenital heart disease • Duodenal stenosis or atresia • Imperforate anus • Hirschprung disease	Growth retardation & obesity	
CNS • Hypotonia	Developmental and mental retardation Decreased sensitivity to pain	Decrease in cognitive function Alzheimer's disease
Immune and Haematopoietic systems • Transient myeloproliferative disorder	Leukaemia Immune effects and/or infection	Male sterility
Other	Thyroid dysfunction	Reduced longevity

Table 1:Major components of the phenotype of Down Syndrome

From the above table, it could be isolated that varied dysmorphic features have been accelerating the dysmorphic condition of DS where oxidative stress generation has been leading the growth of other similar situations among the child and even in the adulthood. These rapid growths of pathologies are not only the result of a single trisomy rather it regards as a multigene disorder. According to Stylianos *et al.* (2006), the genetic basis for DS is trisomy 21 has been evident with the presence in the genome of three rather two chromosomes 21 – and this has

three immediate implications. The first implication is that several genes are likely to be involved where a major phenotypic effect on various genes are involved in determining the type of DS. Hence, literature justifies that DS is not only a single chromosome disease rather various qualitative factors even impact them. Thus, this raises the question of how such a relatively modest increase in gene expression can have such deleterious consequences.

On the other hand, implication has been even found in functional non-protein-coding DNA elements that have been involved. A comparative analysis of human with other vertebrate genomes revealed the presence of conserved regions that have been not the part of annotated genes. These sequence of coding and non-coding protein disagreement and actual pathogenesis of DS have been still a mystery for the scholars and hence thus the question for adequate pathogenesis is required for management and protection.

Need for the study: -
We are observing ever increasing cases of Down Syndrome. It's essential to study Down syndrome as it presents unique challenges and opportunities. Despite medical advancements and increased awareness, individuals with Down syndrome still face various health risks and societal barriers. Understanding the underlying causes, improving early detection, developing effective interventions, and promoting inclusive policies are crucial in addressing these challenges.

Hypotheses: -
H 0 - There is no relationship between oxidative stress and down syndrome

H 1 - Irrespective of the age or advanced age of pregnancy, social factors create oxidative stress.

Aims: - This research aims to evaluate the causes of Down Syndrome as well as plan an effective management policy differentiating constitutional and generalized approach

Objectives: -
- To find out the root cause of Down Syndrome
- To ruled out the exact cause how oxidative stress impact in Down syndrome
- To ruled out the exact cause how delayed pregnancy or advanced age of pregnancy impact in Down Syndrome

Methods & Materials
Study Groups: Parents of different age group, sex, religion, economic condition, occupation, and geographic condition have been selected as the study group. Apart from this, families where DS has been evident have been even analysed in order to provide a comparative analysis method that could differentiate the growth and pathogenesis of DS among different families.

Group	Characteristics	Family Type	No. of participants
A	Married group within 30 years of age	Nuclear	250
B	Married individuals above 30 years of age	Nuclear	300
C	Married individuals above 30 years of age	Joint	350
D	DS patients evident in couples married above 30 years of age	Nuclear + joint	300
E	DS patient evident in couples married within 30 years of age	Nuclear + Joint	160
Total			1360

Table 2: Study Groups

Research Approach: This research is based on the aspect of clinical analysis where detailed case history taking with MSE have been evaluated. The following format has been considered in the work.

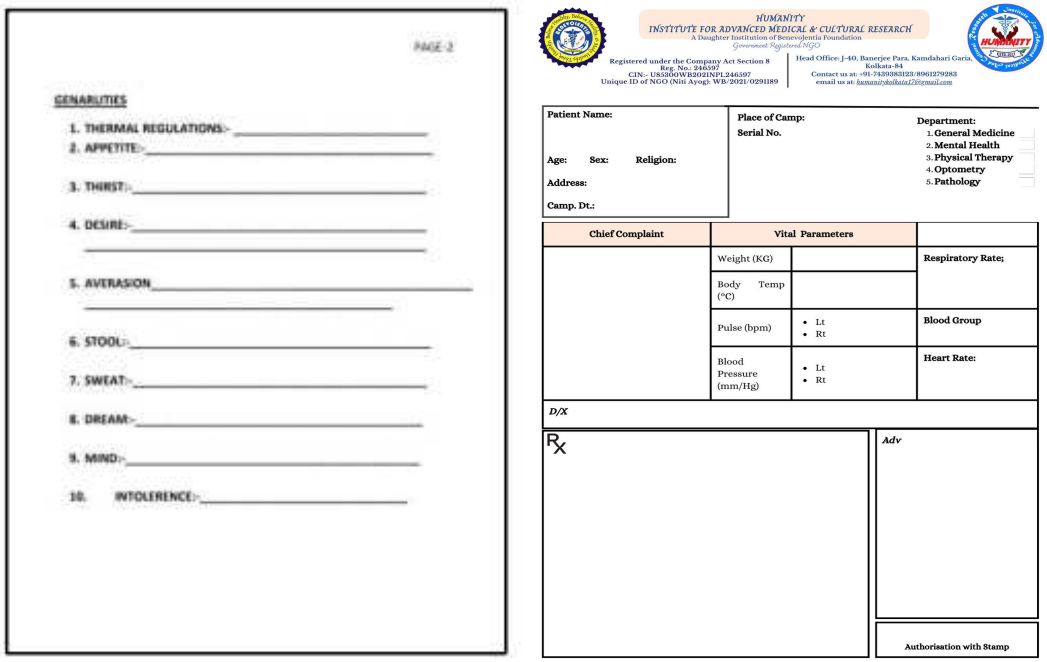

Figure 2: Format for case taking and study design

Based on the approach of above case history taking different aspects of physical and mental assessment have been gathered along with. However, the MSE or mental status examination has been based on the sequence of analysing anger, communication, memory, intelligence and other judge, mental emotions evident among varied groups.

Results

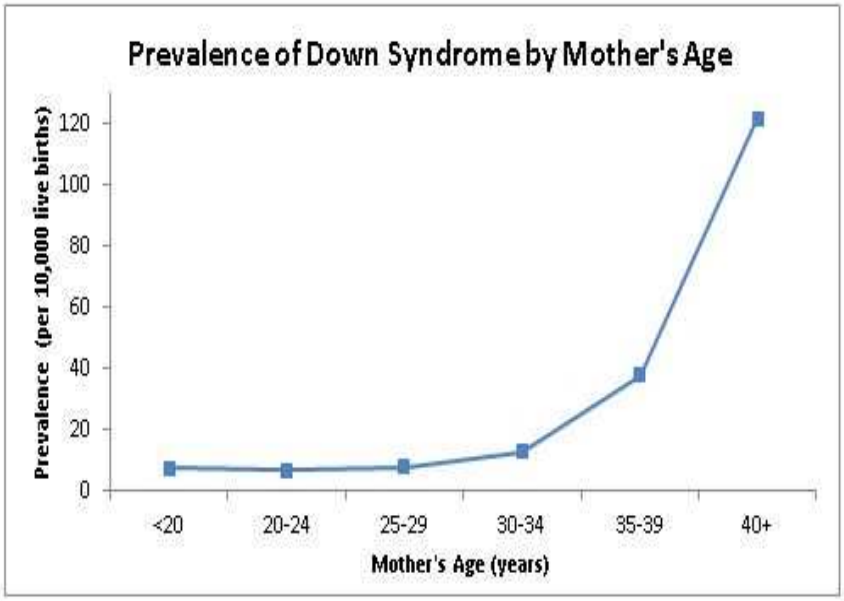

Figure 3: Prevalence of Down Syndrome by Mother's Age

From the above image, it could be described that the equivalence of mother's age in the prevalence of down syndrome. Here, the maximum prevalence could be evident in the mothers above the age of 35 years. This equivalently justifies that there is a relation between the quality of life and age of pregnancy among the women is essentially affecting the growth of Down Syndrome (DS).

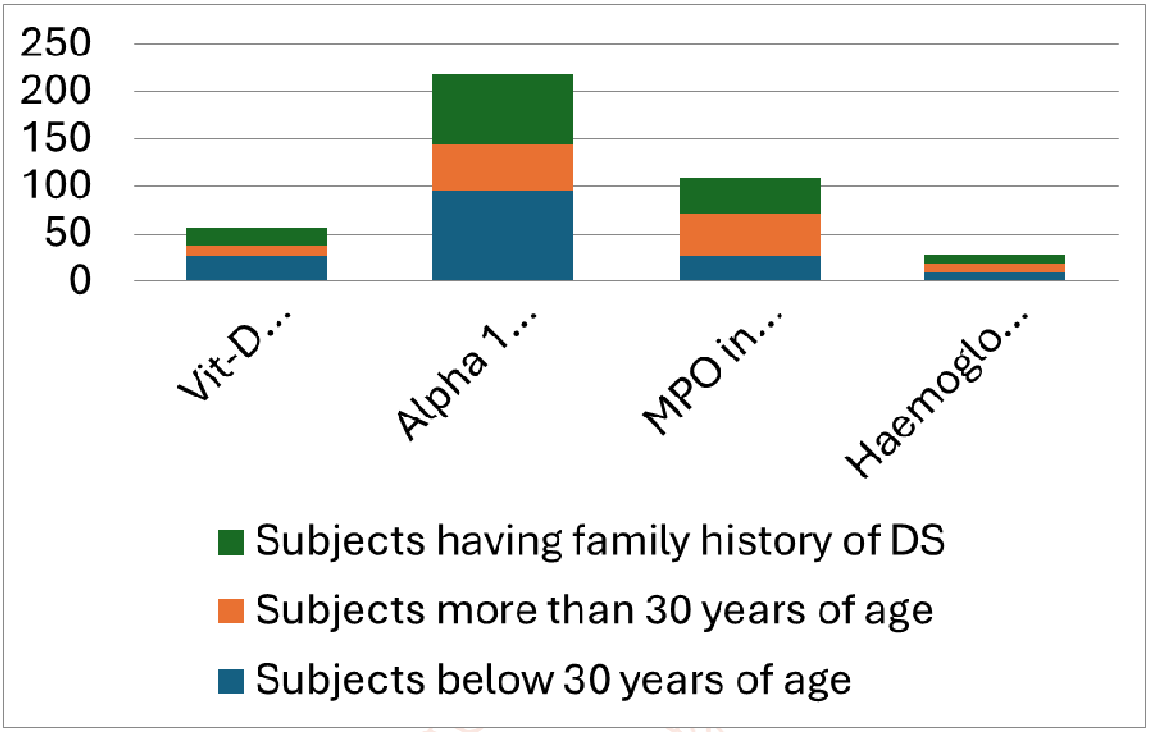

Figure 4: Comparative Analysis between three groups in different subjects

The above chart comparatively relates the aspects of varied anti-oxidants and submerged oxidative stress parameters that have been affecting the generation of DS. In nexus with this, Vitamin D level, Alpha-1-antitrypsin, MPO, and Haemoglobin differentiation have been subjected to change in different parental groups. Furthermore, it has been evident that the biochemical parameters among the subjects having family history of DS and subjects more than 30 years of age have similar ranges of differentiated levels affecting the further generation suffering from not only DS rather varied other sets of genetic or phenotypic disorders.

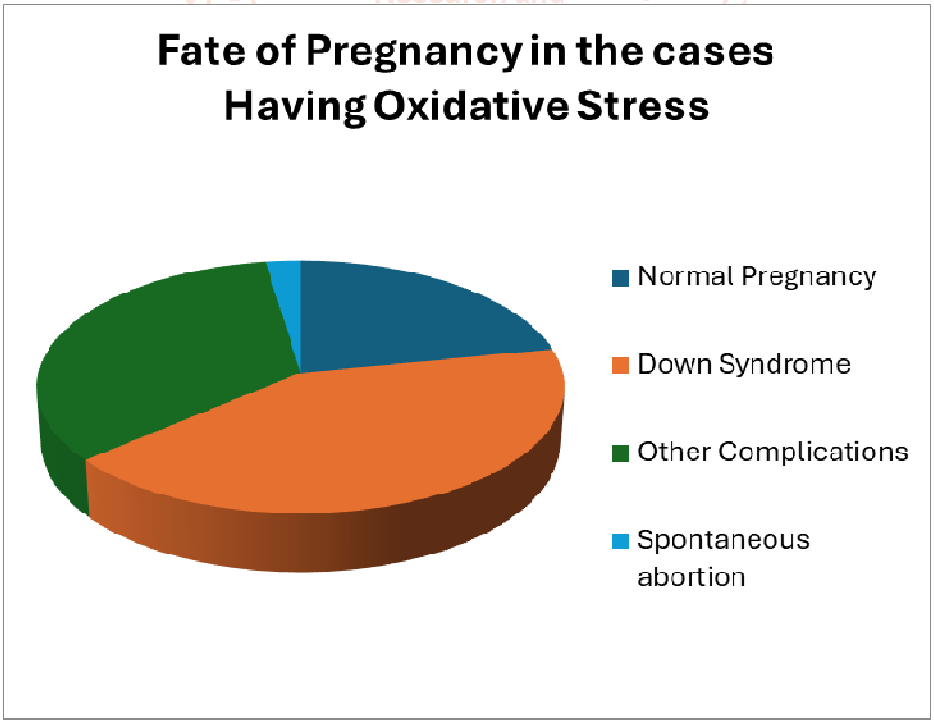

Figure 5: Fate of Pregnancy in Cases having OS

The generation of oxidative stress among different group of the study evident that majority of OS among the pregnant women in evident in the DS suffering child where other complications have been even evident. Although in case of spontaneous abortion range of OS have been even affecting the mother's health; thus, the major aetiological factor for pregnancy complications arises with the dissociation of oxidative stress leading to varied factorial issues.

Discussion

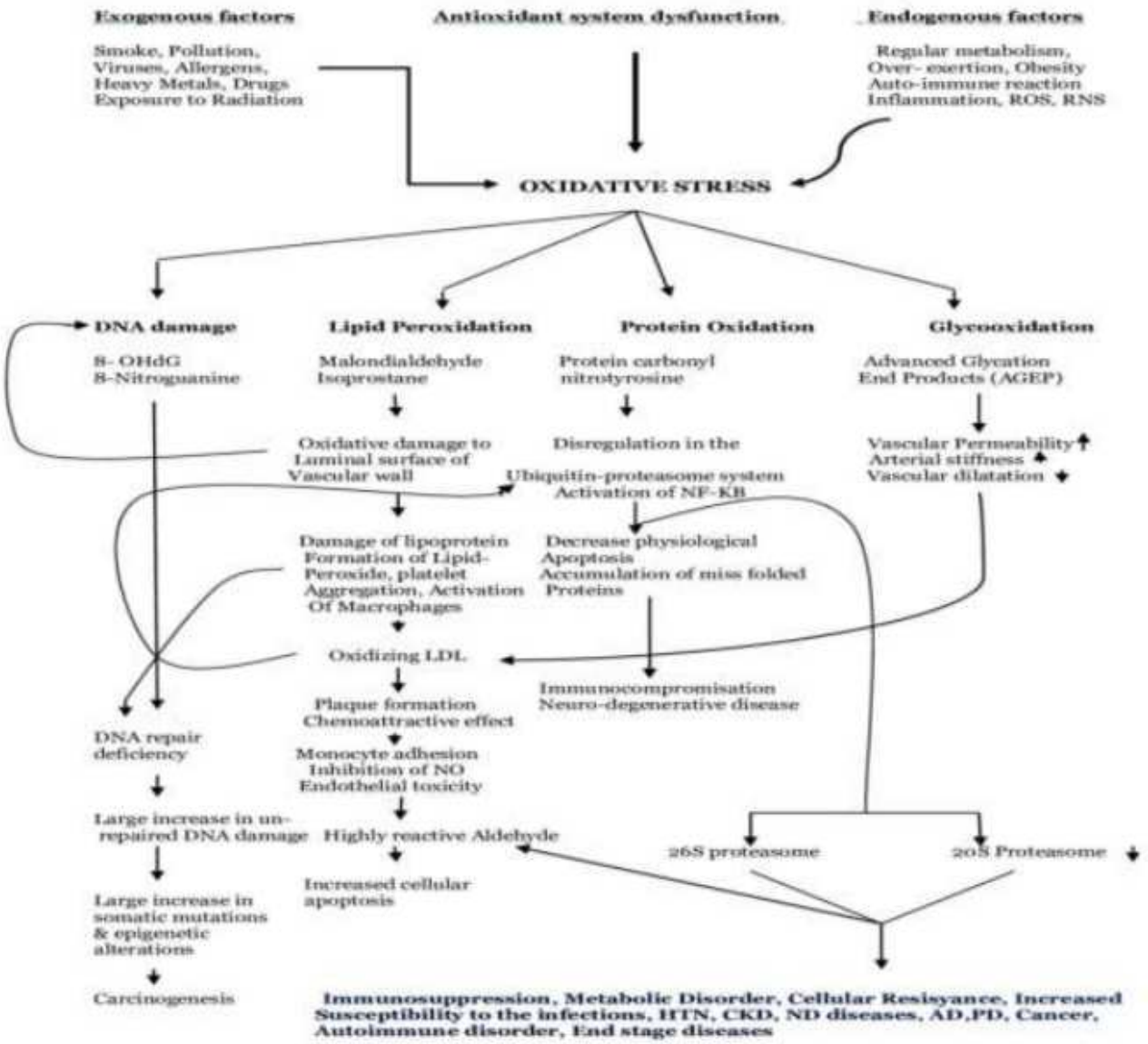

Figure 6: Aspects of Oxidative Stress
(Source: Das *et al.,* 2020)

As evident from the research study results, oxidative stress has been found to be the major issues leading to the generation of DS in the children. The above chart justifies the aspect that generation of DNA and Genomic damage in the mothers with the growth of oxidative stress as evident in the results of biochemical parameters. In nexus with this, other associated issues such as lipid peroxidation, protein oxidation and glycoxidation have been significantly leading to the generation of other adaptive pathologies that could be expressed in next generation.

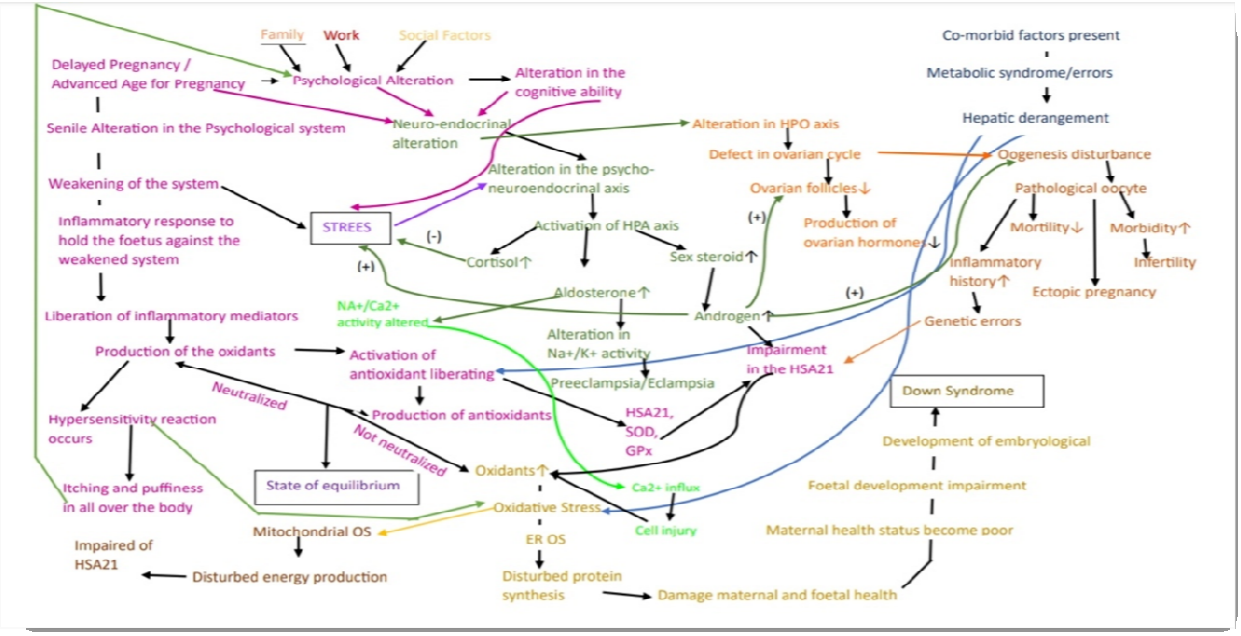

Figure 7: Pathogenesis of Down Syndrome through Oxidative Stress

The above pathogenesis clearly identifies the advent of DS among the child as not only a multigene disorder rather varied changes in the cell cycle and the human body that alternatively affects the embryological development. However, from the chart it could be identified that family, work, social factors, co-morbid factors, delayed pregnancy, or advanced age pregnancy have been the major causes for the development of neuro-endocrinal alteration. This change is hence further evident with the disrupted state of equilibrium that increases the risk of mitochondrial OS generating cell injury and DNA damage memory. This transmission of DNA damage has been correlated with the dysregulation of cell cycle that further leads to chromosomal network damage. Hence, DS is not only a disease related to the trisomy of 21 chromosome rather there are various physiopathological aetiologies that gathers along with the development of such disarrangement.

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