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RESEARCH ARTICLE

A SYSTEMATIC REVIEW ON THE PREVALANCE AND MANAGEMENT OF JAUNDICE THROUGH DIETARY MODIFICATIONS

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ABSTRACT

The objective of this study is to find the widespread prevalence of the disease across the world along with its causes, people who all are affected and results of this disease. Jaundice is most severe in Asian male babies along with the Native American babies; both are found to be the most affected ones with the neonatal jaundice followed by Caucasian ones which are further followed by the African ones. So, it's necessary to know about jaundice in different age groups and what can be the preventive measures like dietary modifications and controlling other health conditions and other factors so as to avoid the disease or at least lowering the impact of the disease. Avoidance and early curing of the disease is the main motto of the research. Common symptoms of the disease include yellowing of skin and white part of the eye, colored feces, itchiness and dark colored urine. This disease shows gradual symptoms as the bilirubin level in the blood increases. It may take up to 3 days to show the symptoms. Most commonly it affects infants of age 0-3 days but its affect can be seen in people of almost all age groups. This is one of the most widespread diseases across the world and if left untreated, may result in death and hence this study is made which focuses on the prevalence, management and dietary modifications of the disease.

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INTRODUCTION

The liver removes out toxins from our body and bilirubin (a waste product remains in the blood after the removal of haem [iron] group from the hemoglobin of Red Blood Corpuscles) is one of them. In liver bilirubin gets conjugated with other chemical substances and forms conjugated bilirubin, which is secreted in the bile and is then excreted in stools, giving stools it yellowish or brownish color. When there is excess of bilirubin, it leaks out in surrounding tissue and is not conjugated and hence known as unconjugated bilirubin. This unconjugated bilirubin is a neurotoxin which can cause death and neurological sequelae in severe cases and may lead to yellowish pigmentation of the skin color in normal cases and the disease is known as jaundice.^[1] In jaundice, the color of the skin changes to yellowish or greenish, this yellowing of the skin is first visible on the face and forehead and then is seen on the trunk and extremities especially of neonates.^[47] Along with the skin, pigmentation of the sclera (white part of the eye)

also takes place. This pigmentation is a result of high bilirubin level. Other symptoms include pale colored feces, itchiness and dark colored urine. Jaundice affects almost all age group individuals. Jaundice occurs in small babies most commonly within the first week of the birth and if continues for a long time, then it may cause kernicterus (a type of brain damage).^[2] Jaundice not only affects the liver, but the whole body. Jaundice is broadly categorized into four major types namely – Neonatal jaundice (caused in newborn babies within a few days of birth), Hemolytic jaundice (caused as a result of breakdown of red blood cells), Obstructive jaundice (caused due to obstruction or blockage of bile ducts), Hepatocellular jaundice (caused when the liver fails to produce bilirubin).^[3] Jaundice can be diagnosed by a number of tests referred to as LFT (Liver Function Test) which include total bilirubin count (if levels of bilirubin are increased then it is referred as jaundice), conjugated bilirubin count (is found to be increased during jaundice), unconjugated bilirubin count (is found to be increased during jaundice), urobilinogen (unlike the previous tests it gets decreased during jaundice as urobilinogen is the product formed during the process of reduction of bilirubin^[4]), along with these tests urine color and stool color are also

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examined which are found to be dark yellow and pale yellow respectively, with the presence of conjugated bilirubin in the urine. During jaundice alkaline phosphatase levels increase with the increased levels of alanine transferase and aspartate transferase.^[5]

Background

Due to a number of reasons jaundice is more prevalent in developing countries as compared to that of developed countries. Since 2006, a number of outbreaks have been seen in countries like India, Pakistan, Bangladesh, etc. In different parts of India, many outbreaks of jaundice have been seen like in Girdharnagar, Ahmadabad, Gujarat in the year 2008 it was found that approx 10.9/1000 people were suffering from jaundice being a total of 233 cases of jaundice. People of all age groups were affected 20-29 years being the most common one with the attack ratio of 18.5/1000.^[6] Just like this, another outbreak was seen in Shimla, Himachal Pradesh, according to official estimates, during the period of four months, i.e. from December 2015 to March 2016 there were about 1600 cases of jaundice with 10 deaths. While if we go through unofficial records the number increased to 10,000 from 1600 making half of the Shimla affected with jaundice.^{[7] [8] [9]} In the Kangra district of Himachal Pradesh a total of 100 cases have been reported in December 2014.^[21] In the regions of Malappuram, Vattankulam, Pandikkadu, Manakda and Mambad, Kerala, a total of 236 cases of jaundice were reported in 2016. 65 cases of jaundice along with one death were recorded alone in Kavanoor Panchayat of Malappuram.^[10] The 2014 Sambalpur jaundice outbreak^[11] is one of the most heard outbreaks in India. Within a period of six months, i.e. from September 2014 to February 2015 it spread to almost all parts of the Odisha. In November, about 20 cases were reported daily along with 6 deaths the case count reached to 677^[12] and by the end of the year the number of cases grew to 1,547 people with 17 deaths.^[14] By the mid of February the total number of jaundice cases across the state reached to 3,966 with an official death count of 36 and unofficial death count being 50.^{[13] [15] [16]} In May 2012, a similar outbreak was observed in Kohlapur, Maharashtra a total of 3,803 cases along with 12 deaths has been registered among which 70% being pregnant women.^[17] In Batala, Punjab 42 people have been diagnosed with jaundice in February 2016^[18] while a total of 33 people have been affected in the locality of Jalandhar in May 2015.^[19] About 18 cases were reported from the Phagwara district of Punjab among which mostly were children below the age of ten years.^[20] In Ambala city of Haryana 12 cases were reported in March 2005^[22] while in Fatehabad a total of 25-30 cases have been reported in April 2010, the statistics being unofficial (officials claim the recorded cases to be 4-5).^[23] 1526 students were found to be affected with jaundice in the hostel campus of Central University of Rajasthan, Kishangarh, Ajmer, India during the months of October and November 2014. Overall, 71.5% were males and 28.6% were females were affected with jaundice in different parts of Rajasthan, while a total of 4.5% males residing in university and 2.5% females residing in university were affected.^[24] Many studies show that about 25-50% of all the babies born in India develop jaundice, thus making the percentage of neonatal jaundice to be high.^[25] As a whole there were about 804,782 hepatitis cases (all leading to jaundice) and 291 outbreaks were reported from different parts of the country.^[26] In the neighboring countries of like Pakistan about 446 among 1690 (27.6%) infants are affected with

jaundice. These infants were found to have high bilirubin levels in few initial days and among these infants 64% were 0-6 days old.^[27] In Bangladesh, in year 2005-2008 a total of 426 (22%) cases of jaundice in neonates were reported.^[28] It was also found that among all maternal deaths 19% to 25% accounts for jaundice while neonatal deaths account for 7% to 13% deaths in Bangladesh.^[29] Just like Pakistan and Bangladesh, Nepal also faces the epidemic of jaundice. Between the years 2005 – 2008 86 neonates suffering from jaundice were admitted to the ICU of Nepal Medical College Teaching Hospital, Attarkhel, Kathmandu.^[30] Another study conducted from May 2003 to January 2006, on 18,985 infants born in Sarlahi district of southern Nepal shows that of the total cases the percentage of neonatal jaundice was found to be 29.3 per 1000 live births.^[31] In 2013, it was found that neonatal jaundice was responsible for 46% cases in Myanmar, some leading to death as well.^{[32] [33]} Studies reveal that infants born to Asian mothers are more prone to neonatal jaundice as compared to that of others. A total of 1680 infants were studied of which 48.8% infants born to Asian mothers were suffering from or suffered from neonatal jaundice within few days of their birth.^[34] After a number of studies in Australia, the estimated cases of neonatal jaundice were found to be between 7.1 and 45 per 100,000 births making it a rare disease.^[35] A study conducted in Sweden, Europe it was found that out of 1019220 births between year 1987 to 2002, 0.6% infants i.e. 6,057 of the infants were affected with hemolytic jaundice whereas, 3.6% infants i.e. 36,869 of the infants were affected by non-hemolytic jaundice.^[36] In Lagos, Nigeria, South Africa, out of 5,262 only 48.7% infants were born in hospital among which 6.7% suffered from neonatal jaundice.^[37] Another study, which took place at University College Hospital, Ibadan, Nigeria, South Africa states that during a time period of ten years (January 1, 1992 – December 31, 2001) the number of registered pregnancies were found to be 16,566 among which 52 cases were reported of jaundice, making an overall count of 0.3% or less than 1%.^[38] In Canada, USA 45.5% infants had signs of jaundice while 3.2% were readmitted to the hospital due to jaundice.^[39] Asian male babies along with the Native American babies are found to be the most affected ones with the neonatal jaundice followed by Caucasian ones which are further followed by the African ones.^[46] Globally, jaundice occurs more in developing countries as compared to that of developed countries.

Causes

Major causes of neonatal jaundice being liver diseases like hepatitis, viral hepatitis, hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, hepatitis G, hepatitis X, autoimmune hepatitis, liver failure, cirrhosis. Causes of hemolytic jaundice are hemolytic anemia, Rh incompatibility, and malaria. Causes of obstructive jaundice are bile duct obstruction, gallstones, biliary system tumor, biliary infection, gallbladder cancer, bile duct cancer.^[40] Apart from these in a developing country like India other causes being the use of unhygienic living conditions; polluted and unsafe drinking water.^[41] After studying the tribal population of India, it was found that the deficiency of G6DP (Glucose-6-Phosphate Dehydrogenase) causes jaundice not only in neonates but also in adults.^{[42] [43]}^[44] Viral hepatitis is also found to be the culprit among the Indian population; a surveillance program took place across the country and was found that almost all the cases of hepatitis suffered from jaundice either severe or moderate. A total of

804,782 hepatitis cases were reported all leading to jaundice as their primary symptom.^[45] Neonatal jaundice is observed 20% more in preterm infants i.e., 80%, while in full term infants the chances of jaundice are lesser being 60%. The signs of jaundice can be seen within first three days of the birth of the baby. It has also been found that the babies who are fed on formulas and other milks tend to have a lesser risk of jaundice as compared to that of breastfed ones.^[50] Underdeveloped and big babies are more at a risk of having neonatal jaundice as compared to that of normal ones.^[46] It was also found that factors like fetal sex, birth weight, and maternal hemoglobin along with the mode of delivery don't have any appreciable impact on the bilirubin levels of the infant. A study conducted on fifty pregnant mothers and their fifty two new born babies (mothers with complicated pregnancy and new born babies with congenital or genetic abnormalities were excluded; only the normal deliveries were taken into consideration.) reveals that there is a more chance of getting jaundice to baby born to bipara mothers (mother who is giving birth to second child) as compared to that of primipara mothers (mother who is giving birth to first child) and multipara mothers (mother who is giving birth to third or fourth child).^[48] In another research on 400 icteric neonates, it was found that 5.8% (23) were suffering from urinary tract infection, 1.3% (5) have G6PD deficiency 4.8% (19) have dysmorphic Red Blood Cells while 0.75% (3) have ABO or Rh incompatibility making them as a cause of jaundice in India.^[49] In country like Pakistan, the major causes for jaundice are found to be hepatitis C virus in which many of the patients suffered from moderate to severe jaundice.^[51] Other cause found in Pakistan is malaria caused due to *P. falciparum*, in a research on 76 patients of malaria 35 (46.05%) developed jaundice while others have an increased level of serum bilirubin, which may at any stage of the disease lead to jaundice.^[52] Another reason found from studies is gall bladder cancer, which majorly causes jaundice in 49.8% of 245 patients.^[53] Many other causes have been found to be the reason of jaundice in Pakistan like G6PD deficiency,^[54] Bile acid-CoA ligase deficiency,^[55] Moving to Bangladesh, the causes of jaundice in Bangladesh are found by a study conducted on 1981 neonates in the Khulna Medical College Hospital in Bangladesh. The results of this study revealed that the causes of hemolytic jaundice are ABO incompatibility and Rh incompatibility and the infants who were more susceptible to jaundice are either underweight or preterm infants.^[56] In Nepal, the major causes of neonatal jaundice are septicemia, prematurity and ABO incompatibility.^[30]

Apart from these, the other factors leading to jaundice are male sex, high birth weight, breastfeeding patterns, warm air temperature, primiparity (mother who is giving birth to first child), skilled birth attendance, place of delivery, prolonged labor, oil massage, paternal education and ethnicity were significant risk factors. In infants with feeding difficulties, exclusive breastfeeding was among the factors leading to neonatal jaundice, exclusive breastfeeding was found to be helpful in infants without any difficulty in feeding exclusive breastfeeding was found to be helpful.^[31] In China, from a study of 1238 full term infants the cause of jaundice is found to be in infants who are ABO incompatible with that of their mothers along with the deficiency of G6PD enzyme and preoperative biliary drainage (PBD) leading to malignant obstructive jaundice.^[59] Other factors associated with the risk of leading to jaundice are male sex, elder sibling with the history of jaundice and breastfed infants. Factors which don't

have an impact on the disease are gestational age, mode of delivery, weight of an infant at the time of birth, augmentation of labor.^[57] Similar factors are found to cause jaundice in Myanmar (G6PD deficiency).^[58] In Asia, after a number of studies the major factors leading to jaundice are neoplasia, common bile duct stone,^[60] ABO incompatibility, G6PD enzyme deficiency, Rh incompatibility (rarely), polycythemia (rarely),^[61] malignant carcinoid tumors^[62] biliary cast syndrome,^[63] apart from hepatitis,^[40] unhygienic living conditions.^[41] In other continents like Europe, the major reasons for the cause of jaundice are hepatic infection caused due to infection by *Fasciola hepatica*,^[64] deficiency of uridine diphosphate-glucuronosyltransferase (B-UGT) which is a rate limiting enzyme in the process of conjugation of bilirubin with glucuronic acid which is finally excreted in bile;^[65] abdominal tuberculosis, i.e., pancreatic and hepatic tuberculosis^[66] malignant gastrointestinal stromal tumor (GIST),^[67] syphilis, fatty liver.^[68] Hepatobiliary cystadenomas (HBC) and cystadenocarcinomas rarely also cause jaundice.^[69] Neuroblastoma also rarely acts as the precursor to jaundice in European countries.^[70] Both haematolytic and non haematolytic jaundice are found to have different risk factors in Europe, for haematolytic jaundice the major risk factors are maternal alloimmunisation (alloimmunisation is the immune response to foreign antigens after exposure to genetically different cells)^[71], blood group O and neonatal jaundice in the older sibling while for the non haematolytic jaundice the risk factors include preterm birth, neonatal jaundice in the elder sibling, maternal obesity and maternal origin from south-east Asia.^[72] The major cause of jaundice in Australia is found to be ABO incompatibility and other blood related incompatibilities like Rh incompatibility; glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency), infection, haemolysis, spherocytosis (formation of sphere shaped RBCs rather than biconcave disk shaped). Other factors are also found to have influence on jaundice and they are male gender, premature birth, early hospital discharge, breastfeeding.^[73] From studies causative factors and factors increasing the risk of jaundice in South Africa are found to be infant's gender, maternal religion, weight at the time of screening, place of birth, multiple gestation, use of herbal preparations during pregnancy, exclusive breastfeeding^[37] Other diseases like viral hepatitis, malaria, sickle cell anemia, sepsis, cholestasis, pre-eclampsia, preterm delivery, intrauterine fetal death (IUFD) are also found to be one of the reasons of jaundice.^[38] But the case is totally different in the American continent, where acute viral hepatitis is no longer a common cause of jaundice in the pregnant ladies. The current causes of jaundice over the American continent are found to be gallstones and preeclampsia-related disorders.^[74] Globally, it can be concluded that the major reasons for the cause of hepatitis are gall bladder stones, viral hepatitis, malaria, G6PD enzyme deficiency,^[75] unhygienic living conditions, breastfeeding, ABO incompatibility.

Conclusion

From above review of literature it can be concluded that jaundice is a wide spread disease and its patients can be seen in almost every nook and corner of the world. It can be checked with the initial symptoms like yellow of the skin and sclera, and other symptoms include pale colored feces, itchiness and dark colored urine. It is majorly of four types – neonatal, obstructive, hepatocellular and hemolytic. It is

caused by a number of factors like hepatitis, viral hepatitis, hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, hepatitis G, and hepatitis X, autoimmune hepatitis, liver failure and cirrhosis. Causes of hemolytic jaundice are found to be hemolytic anemia, Rh incompatibility, and malaria. Causes of obstructive jaundice are bile duct obstruction, gallstones, biliary system tumor, biliary infection, gallbladder cancer, bile duct cancer. The harmful effects of disease can be minimized by proper medications and dietary management. Diet therapy along with medications proves to be very helpful for the early recovery of the patient. The calorie intake of the patient totally depends on the condition and severity of the disease. Initially, the calorie intake is to be about 1000 Kcal/day and after three or four days the calorie intake is increased to 1500Kcal/day and then finally according to the Recommended Dietary Allowances. Initially carbohydrates which are to be provided are should be simple carbohydrates in the form of fruit juices (sugarcane juice), soups, water and electrolytes so as to flush toxins (bilirubin) from the body along with the urine. After 4-5 days, when bilirubin's levels start dropping fruits like watermelon, melon, orange; green leafy vegetables (slightly boiled); yogurt; custard can be given. The carbohydrate content in the diet should be high so as to prevent the breakdown of proteins from the tissues. As steatorrhea (presence of excess fat in the stools) is the common symptom during the jaundice, fat intake is restricted and only essential fatty acids like omega-3 and omega-6 fatty acids are to be given. Adequate amount of protein is given. Small and light meals are preferred so as to lessen the burden on liver as our liver is still in recovery phase and electrolyte and fluid balance is to be maintained due to loss by excess urination. [76] In infants (age- 0-6 months) formula feeding is preferred over breast feeding as formula feeding reduces the risk of neonatal jaundice and helps in early recovery. [77] Thus, after studying the literature it can be stated that if the person is treated with diet therapy along with the medications in the initial days, harmful effects of the disease can be avoided and an early recovery is observed.

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