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Role of *Krimi* (Pathogen) in *Aupasarkika Yakrit Vikara* (Infective Liver diseases) - A Narrative Review

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ABSTRACT

Infective liver diseases are more than 18% of total Chronic Liver Diseases and been ranked as the fifth most common cause of death worldwide. *Krimi* can create systemic infection like - *Jvara*, *Vibarnata* (skin rash), *Shula* (Pain), *Bhaktadwesa* (anorexia), *Krimija Pandu* (Anaemia) etc. to organ specific disorders like - *Krimi Danta*, *Krimi Karna*, *Asadhya Pratisyaya*, *Krimi Granthi*, *Krimija Hrudroga*, *Krimija Shira Roga* But *Krimijayakrit Vikara/Roga* is not found in classical literature. A considerable number of Infectious liver disease patients came to various Ayurveda Hospital and expert Ayurveda physicians either feed up with conventional treatment or cannot bear the expenses of conventional therapy. Therefore, it is an attempt to establish the role of *Krimi* in *Aupasarkika Yakrit Vikara* through reviewing Ayurveda and modern literature with some experience-based inputs. Virus, bacteria, protozoa can be *Adrisya Krimi* (not visible in necked eye), *Anu* (minute) and *Suksma* and Nematodes and fungus are *Drisyaya* (Visible) *Krimis*. *Purisaja* and *Raktaja Krimi* can produce *Krimija Yakrit Roga* as near to Liver and through gut - liver axis and rich circulation of liver. *Jvara* (Fever), *Shula* (abdominal pain), *Mandagni* (low digestive power), *Pita Netrata* (Jaundice) are cardinal symptom of *Krimija Yakrit Roga*. In three dosas, *Kapha Dosa* is more aggravated in *Krimija Yakrit Roga*. *Rakta Vaha Srotas* and *Purisha Vaha* are mostly affected *Srotas* in *Krimija Yakrit Roga*. *Sahaja Krimi* or *Avaikarik Krimi* are said to be gut microbiota which are more than 100 trillion microorganisms in the gut show high metabolic activity and are continuously helping with the host immune system through gut-liver axis. *Krimija Yakrit Roga* can be a type of *Yakrit Roga* which clinically manifested as *Yakritdalludara* (Hepato megaly) and *Yakrit Kshyaya* (Cirrhosis of Liver). Successful diagnosis of type of *Krimi* can be possible though careful history and appropriate microbial and radiological studies for proper treatment of liver diseases.

Key words: *Krimija Yakrit Roga*, *Purisaj And Raktaja Krimi*, *Sahaja Krimi*, *Adriswa Krimi*, *Yakritdalludara*, *Yakrit Kshyaya*.

INTRODUCTION

Krimi in Ayurveda is having broadsense of pathogen that includes all worms and microbes causing infection as well as maintain health in Human. Ayurveda narrated infectious diseases as *Aupasarkika*

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Roga which can transmit one person to other through touching body, inhalation of droplet, sexual contact, eating together and exchange/sharing bed, garland, dress etc. It can be said that *Krimi* can transmit in the personal contact and droplet and create *Aupasarkika Roga* (Infectious diseases) in general. *Krimi* can create systemic infection like - *Jvara*, *Vibarnata* (skin rash), *Shula* (pain), anorexia, *Krimija Pandu* etc. to organ specific disorders like - *Krimi Danta*, *Krimi Karna*, *Asadhya Pratisyaya*, *Krimi Granthi*, *Krimija Hrudroga*, *Krimija Shira Roga* but *Krimijayakrit Vikara/Roga* is not found in classical literature.^[1] Although Maharsi Harita explained habitat and shape of *Krimi*, that mostly found in *Kaphasthana* (Organ with predominant with *Kapha*) and *Maladhara Kala* (mucous membrane of GI track). The shape and size of Internal *Krimis* are also explained as *Pruthumunda* (Broad /square shape), *Kanchuka* (rounded shape),

Dhanya Kurnibha (sprouted pulse with white appearance), *Susma* (Invisible), *Anu* (Minute) and *Suchimukha* (Tapered mouth).^[2]

Infectious liver diseases are unambiguously one of the major contributors of liver diseases world wide despite of development of vaccine, antibiotics, antiviral and other anti-protozoan, anti-helminthic, anti-fungal agents etc. Liver disease rates has been steadily increasing over the years in spite of good awareness. According to National statistics in the UK, liver diseases have been ranked as the fifth most common cause of death.^[4] The global incidence of infective liver diseases is are than 18% of total CLD cases. A considerable number of Infectious liver diseases patients came to various Ayurveda Hospital and expert Ayurveda physicians either feed up with conventional treatment or cannot bear the expenses of Conventional therapy. Therefore, it is an attempt to establish the role of *Krimi* in *Aupasarkika Yakrit Vikara* through reviewing Ayurveda and modern literature with some experience-based inputs.

MATERIALS AND METHODS

A literature survey from Ayurveda classical texts were undertaken to find out the link of *Krimi* in Liver disease's pathogen in the light of present understanding of microbiology and pathophysiology of infective liver diseases.

Enumerations

Liver plays an important role in host defence against invasive micro-organism as it receives both portal and systemic circulations and also reserve of reticulo-endothelial cell mass. Virus, bacteria, protozoa, helminths and fungi can infect liver, presenting with wide range of clinical symptoms from asymptomatic with elevated liver enzyme, liver failure, hepatic fibrosis, cyst, abscess, cirrhosis and hepto cellular cancer.^[3] It can be narrated as *Suksma* and *Anu Krimi* causing liver diseases as in Table-1.

The hepatotropic virus (Hepatitis A, B, C, E) infect liver for its replication and organ damage. Other non-hepatotropic virus (Herpes, adeno virus, SARC virus, COVID-19) and other systemic viral infection (Yellow

fever, Influenza, H1N1, dengue) can also be the cause of hepatitis as a consequence of an viral antigen from just a de-arranged liver enzymes to liver failure. Liver involvement in non-hepatotropic and systemic viral infections can range from mildly deranged liver biochemistry to fulminant liver failure. In most of these infections, hepatitis is a major consequence of an immune response to viral antigens with a close association between the presence of viral antigens and inflammatory infiltrates in the liver. Loss of immune control may be responsible for the development of hepatitis in CMV hepatitis and other opportunistic viral infections such as adenovirus. Similar activities may also be involved in SARS-associated hepatitis, COVID-19 which is characterized by focal lobular lymphocytic infiltrates to liver.^[5] The role of Natural Killer cells in control of viral infection is well established and Herbal medicines showing anti fibrotic activities concerned with boosting the activation of hepatic NK cells.^{[6],[7],[8]}

Bacterial systemic infections like - *Salmonella typhi*, *Mycobacterium tuberculosis*, *Brucellosis*, *Q fever*, *leptospirosis*, *syphilis* etc. can impact on liver as like other specific organs. The indirect impact of bacterial infection is sepsis and shock but liver abscesses is very common impact on liver. Hepatic involvement with *Salmonella typhi* (Typhoid fever) occurs via both hematogenous seeding of the liver during bacteraemia periods and from infected reticuloendothelial system. Hepatic manifestations of typhoid fever include incidental findings of hepatomegaly and abnormal liver function tests which occur in 50% of cases. A severe form of disease with jaundice can occur in 0.4-26% of cases.

Table 1: *Suksma, Anu* and other *Krimi* (Pathogen) causing liver diseases.

Virus	Bacteria	Parasite	Fungi
Hepatitis A,B, C,&E	<i>Salmonella Typhi</i>	Schistosoma species (Schistosomiasis)	Candida species
Epstein Barr Virus (EBV)	<i>Mycobacterium tuberculosis</i>	Plasmodium species	Histoplasma cap

		(malaria)	
Cytomegalovirus (CMV)	<i>E.coli</i>	Ameoba	<i>Aspergillus</i> spp
Herpes virus	Brucella species	Liver flukes (trematoda)	
Yellow fever virus	Leptospirosis	Tape worm (cestode)	
Influenza Virus	<i>Q fever</i>	<i>Ascaris lumbricoides</i>	
Dengue virus	Klebsiella species	<i>Echinococcus granulosus</i>	
COVID-19			

The elevations in serum transaminases are usually 3-5 times the upper limit of normal with AST usually being higher than the ALT. The study showed that Twenty three percent of cases have elevations in serum bilirubin and alkaline phosphatase levels are normal to slightly elevated. Mycobacterium tuberculosis infection can also impact on liver. Millitary, granulomatous and localised hepatic tuberculosis are three categories of tuberculosis where hepatic involvement causes abscesses and tuberculoma. Hepatomegaly is also noted in 50% of Brucellosis patients. Q fever is a worldwide zoonotic infection caused by *Coxiella burnetii*, an intracellular gram-negative coccobacillus is also hepatic involvement. Icteric disease(Weil's Disease) is a severe form of leptospirosis disease that develops in 5-10% of cases. In this form, jaundice may occur in the acute phase and last for weeks.^[9]

Many Parasite infections may cause liver pathology and cirrhosis in liver. Schistosoma and malaria are two of the most common parasitic infections globally. Jaundice associated with hemolysis can be observed in severe malarial infection, and hepatic failure can occasionally be seen in patients with severe *P. falciparum* infection. Jaundice in malaria consists of both unconjugated and conjugated bilirubin, which could be caused by intravascular hemolysis of parasitized red blood cells, and hepatocellular dysfunction. Hepatic histological findings may show Kupffer cell hyperplasia with pigment deposition, hepatocyte necrosis and cholestasis. Hydatid liver

disease is caused by infection with the metacestode stage of the tapeworm *Echinococcus*. Liver involvement may occur in about two-third of patients with *Echinococcus granulosus* infection, and commonly can form single cyst. Although a patient has no symptom when the cyst is small (< 10 cm in diameter) and without complication, intra-peritoneal rupture may be frequent and cause abdominal pain. Rupture into the biliary tract may cause biliary colic, obstructive jaundice, or cholangitis. Fascioliasis is a trematode infection caused by *Fasciola hepatica* or *Fasciola gigantica*. Fascioliasis (Liver Flukes) commonly consists of two phases, the acute/invasive and chronic obstructive phase. In the acute phase, common symptoms are fever, pain, hepatomegaly and eosinophilia. After six months of infection it leads chronic infection which is characterized by bile duct obstruction associated with bile duct inflammation and hyperplasia due to the presence of adult flukes. *Ascaris lumbricoides* is an intestinal nematode, and arrives in the liver through the bile duct by a retrograde manner. Migration of adult worms into the biliary tree can cause biliary colic, cholecystitis, cholangitis, obstructive jaundice and secondary liver abscess. Several parasites infest liver or biliary tree, either during their maturation stages or as adult worms. Biliary tree parasites may cause pancreatitis, cholecystitis, biliary tree obstruction, recurrent cholangitis, biliary tree strictures and some may lead to cholangio carcinoma. Ultrasonography of the liver is diagnostic tools in schistosomiasis, hydatid cysts, amoebic liver abscess, ascariasis and other biliary tree parasites showing bile duct dilatation.^{[10],[11],[12]}

Hepatic involvement of fungus like - *Candida* spp., molds, and dimorphic fungi are more common infectious and complications of immunosuppressive therapy and chemotherapy. Fungal infections represent <2% of the total isolates in pus from hepatic abscesses.^[13] Hepatic involvement by fungi occurs almost exclusively in the case of disseminated infection in immunocompromised hosts.^{[13],[14]}

Krimi in Ayurveda prospective

The word *Krimi* means "*Lumpayanti Kida Krimayah Paritah*" (Vachaspatyam 3rd part) which can move or

which are capable to break or injure the surroundings can be said as *Krimi*. The term *Kita*, *Jantu*, *Rakshasa* (which drink blood), *Asura* (which destroy life), *Yatudhana* (which causing pain) etc. synonyms are used for *Krimi* in Ayurveda literature. *Krimis* are live in our body in different organ, some times they are not do harm as described by Charak Samhita as *Sahaja Krimi* or *Avaikarik Krimi*. They live in human body from birth till death and are beneficial to human body. They are numerous in number and live in the buccal cavity, alimentary tract as well as in vaginal canal of female as a normal bacterial flora. *Vaikarika Krimi* are classified into two subgroups as *Bahya Krimi* (external) and other is *Abhyantara Krimi* (internal). Those *Krimi* which live on the skin outside the body are *Bahya Krimi* and those inside the body are *Abhyantara Krimi*. Acharya Charak and Vagbhata have mentioned *Bahya Krimi* while Acharya Sushrut has not mentioned *Bahya Krimi*. Acharya Sushrut has classified *Abhyantar Krimi* in two groups (i) *Drishya* (Visible) and (ii) *Adrishya* (Not visible in naked eye). According to Sushrut, *Sleshmaja* and *Purishaja Krumi* are *Drishya* and *Raktaja Krumi* are *Adrishya*. All Acharyas except Acharya Harita and Acharya Sharangdhar have mentioned total 20 types of *Krimi*. Acharya Harita has described 7 types of *Bahya Krimi* and 6 type of *Abhyantara Krimi* while Acharya Sharangdhar has described total 22 *Krimi* with the addition of two *Krimi* - a) *Snayuka* and b) *Vrana Krumi* each (Table 2). *Raktaja Krimi* habited in the vessels carrying blood. *Shleshmaja Krimi* are usually found in *Amashaya* (stomach) which have tendency to move upward or downward along the gastro-intestinal tract. *Purishaja Krimi* are in *Pakawashaya* (Large Intestine) which usually migrate downward towards the rectum and anus. They may travel rarely towards the stomach resulting in faecal smelled belching and breathing and come out in vomiting. All Ayurvedic texts except Charaka Samhita have described common signs and symptoms for all *Krimis* viz. fever, paleness/rashes of skin, cramping pain, heart trouble, lassitude, vertigo, reduced appetite, diarrhoea, vomiting and gurgling sound in the intestine. Other clinical symptoms of human infected with *Krimi* are suddenly falls down on the ground, malaise and

dyspnoea is found in *Krimija Pandu* is available in Charaka and other Samhitas. Harita Samhita's description is more important as it described more complicated symptoms as found in liver diseases like - *Mandagni* (Low digestion), *Pipasa* (Thirst) and *Peeta Netra* (Jaundice) found in liver (Table 3). According to Acharya Charak, Vagbhat, Madhava Nidana, Bhavaprakash and Vangasen, *Bahya Krimi* are caused due to unhygienic and dirty habits (*Mrijavarjanam*). Harita refers to its origin from sweat, dryness (of skin and or body) and worry (*Yuka* and *Liksha*).^[15] The causes for *Abhyantara Krimi* are consumption of food even during *Ajirna*; intake of excess *Madhur*, *Amla* and *Lavana Rasa*; excess intake of unbowed liquids; *Pishtayukta Ahara*; excess intake of *Mamsha*, *Patrashaka*, *Tila Kalka*.

In Vedas various type of *Krimighna* drugs are described. In Atharvaveda, *Krimighna Dravyas* are described in three types - *Krimi Jambhana* (retarding the activity), *Kriminashana* (inhibiting the growth of *Krimi*) and *Krimighna* (killing the *Krimi*). Worship of *Agni* and *Surya* are said to destroy *Krimi*. Most of *Krimighna* effect come under *Daivavyapasraya Chikitsa* as narrated in Vedas.^{[16],[17]}

Sarva Kriminam Apakarshanaamevaaditah Karya, Tatah Prakrutivighatah, Anantaram Nidanoktanam Bhavanam Anupasevanam Iti ||" (Ch.Vi.7/4).

Acharya Charaka described three basic methods for the treatment of *Koshtagata Krimi* such as *Apakarshana* (Removed by *Vamanadi Panchakarma* and Surgical procedures), *Prakrutivighata* (Breaking the pathogenesis by changing environment), *Nidana Parivarjana* (Avoid the etiological factors). *Shodhana Karma* like *snehan*, *Swedan*, *Asthapana Basti*, *Shirovirechan*, *Virechan*, *Dhumpan*; Consumption of *Nimba*, *Arka* (white), *Karela*, *Koshataki*, *Rakta Shali*, *Tila*, *Sarshapa*, *Kulaththa*, *Yava*, *Mudga*, *Gomutra*, *Madhu*, *Sura*, *Sukta*, *Sauvira*, *Tushodaka*, *Patola*, *Rasona*, *Chitraka*, *Kantakari*, *Vidanga*, *Haritaki*, *Bhallataka*, *Hingu*, *Ajamoda*, *Khadira*, *Devadaru*, *Shunthi* avoidance of worry are treatment procedures, diet, drugs and practices for *Krimi*.^{[17],[18]}

Table 2: Total number of *Krimi* and their types as mentioned in different Ayurvedic classics

SN	Name of the text	<i>Bahya</i> (external)	<i>Abhyantara Krimi</i> (Internal)				Total No.
			<i>Kaphaja</i>	<i>Raktaja</i>	<i>Purishaja</i>	<i>Shlesma Raktaja</i>	
1.	Charaka Samhita	2	7	6	5	-	20
2.	Sushruta Samhita	-	6	7	7	-	20
3.	Vagbhatta	2	7	6	5	-	20
4.	Bhela Samhita	-	-	-			20
5.	Harita Samhita	7					13
6.	Madhav Nidana	2	7	6	5	-	20
7.	Sarangadhara	2+1	7	6	5	1	20+2
8.	Bhava Prakash	2	7	6	5		20
9.	Yoga Ratnakara	2	7	6	5		20

Table 3: *Samanya Rupa* (general symptoms) of *Abhyantara Krimi* (Internal) described in different text of Ayurveda

SN	Name of Symptom	Susruta Samhita	Madhava Nidana	Bhavprakash	Harita Samhita	Yoga ratnakara
1.	<i>Jvara</i> (fever)	+	+	+	+	+
2.	<i>Vivarnata</i> (rashes)	+	+	+	+	+
3.	<i>Shoola</i> (pain)	+	+	+	+	+
4.	<i>Hridroga</i> (heart disease)	+	+	+	+	+
5.	<i>Bhrama</i> (vertigo)	+	+	+	+	+
6.	<i>Bhaktadwesa</i> (anorexia)	+	+	+	+	+
7.	<i>Atisara</i> (diarrhoea)	+	+	+	+	+
8.	<i>Sadana</i> (malaise)	+	+	+	-	-
9.	<i>Chhardi</i> (vomiting)	-	-	-	-	+
10.	<i>Swasa</i> (dyspnoea)	-	-	-	+	-

11.	Vami (Vomiting)	-	-	-	+	-
12.	Jatharagarjanam (Blotting)	-	-	-	+	-
13.	Mandagni (Low digestion)	-	-	-	+	-
14.	Pipasa (Thirst)	-	-	-	+	-
15.	Pitanetra (Jundice)	-	-	-	+	-

DISCUSSION

The liver is exposed to many systemic infectious pathogens including not only hepatotropic but also non-hepatotropic microorganisms through both the systemic and portal circulation. These pathogens may directly or indirectly cause liver injury presenting with various clinical manifestations. Virus, bacteria, protozoa can be *Arusya Krimi* (Not visible in necked eye), *Anu* (minute) and *Suksma* and Nematodes and fungus are *Drusya* (Visible) *Krimis*. *Purisaja* and *Raktaja Krimi* can produce *Krimija Yakrit Roga* as near to Liver and through gut-liver axis and rich circulation. *Jvara* (Fever), *Shula* (abdominal Pain), *Mandagni* (Low digestive Power), *Peeta Netrata* (Jaundice) are cardinal symptom of *Krimija Yakrit Roga*. In three *Dosas*, *Kapha Dosha* is more aggravated in *Krimija Yakrit Roga*. *Raktavaha Srotas* and *Purisha Vaha* are mostly affected in *Krimija Yakrit Roga*.

Sahaja Krimi or *Avaiarik Krimi* are said to be gutmicrobiota which forms a complex microbial community have crucial role on human health . The more than 100 trillion microorganisms in the gut show high metabolic activity and are in continuous dialogue with the host immune system.^[19] Moreover, the gut microbiota is an important source of metabolites, hormones and neuro-mediators that directly regulate gut function and indirectly modulate the function of extra-intestinal organs such as the liver, brain and kidney. The relationship between gut microbiota and the liver is still not well understood; however, dysfunction of the gut mucosal barrier (“leaky gut”) and increased bacterial translocation into the liver via the gut–liver axis probably plays crucial roles in liver disease development and progression. There is

increasing evidence for an adverse role of intestinal dysbiosis in the pathogenesis and progression of many chronic liver diseases (e.g., NAFLD, ALD, immune-mediated liver diseases, liver cirrhosis and hepatic carcinogenesis). Amelioration of the dysbiosis through the use of prebiotics, probiotics and fecal microbiota transplantation improves the gut-barrier function and appears to be a promising new approach to managing chronic liver diseases.^[20] Physician should take care of *Krimi*, *Rogi Bala* (host immunity), *Roga Bala* (diseases state), history of drug therapy, travel history after evaluating liver manifestation.^[21]

CONCLUSION

Krimija Yakrit Roga can be a type of *Yakrit Roga* which clinically manifested as *Yakritdalludara* (Hepato megaly) and *Yakrit Kshyaya* (Cirrhosis of Liver). Successful diagnosis of *Krimi* can be possible though careful history and appropriate microbial and radiological studies for proper treatment of liver diseases.

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